MCV/Q

MEDICAL COLLEGE OF VIRGINIA QUARTERLY
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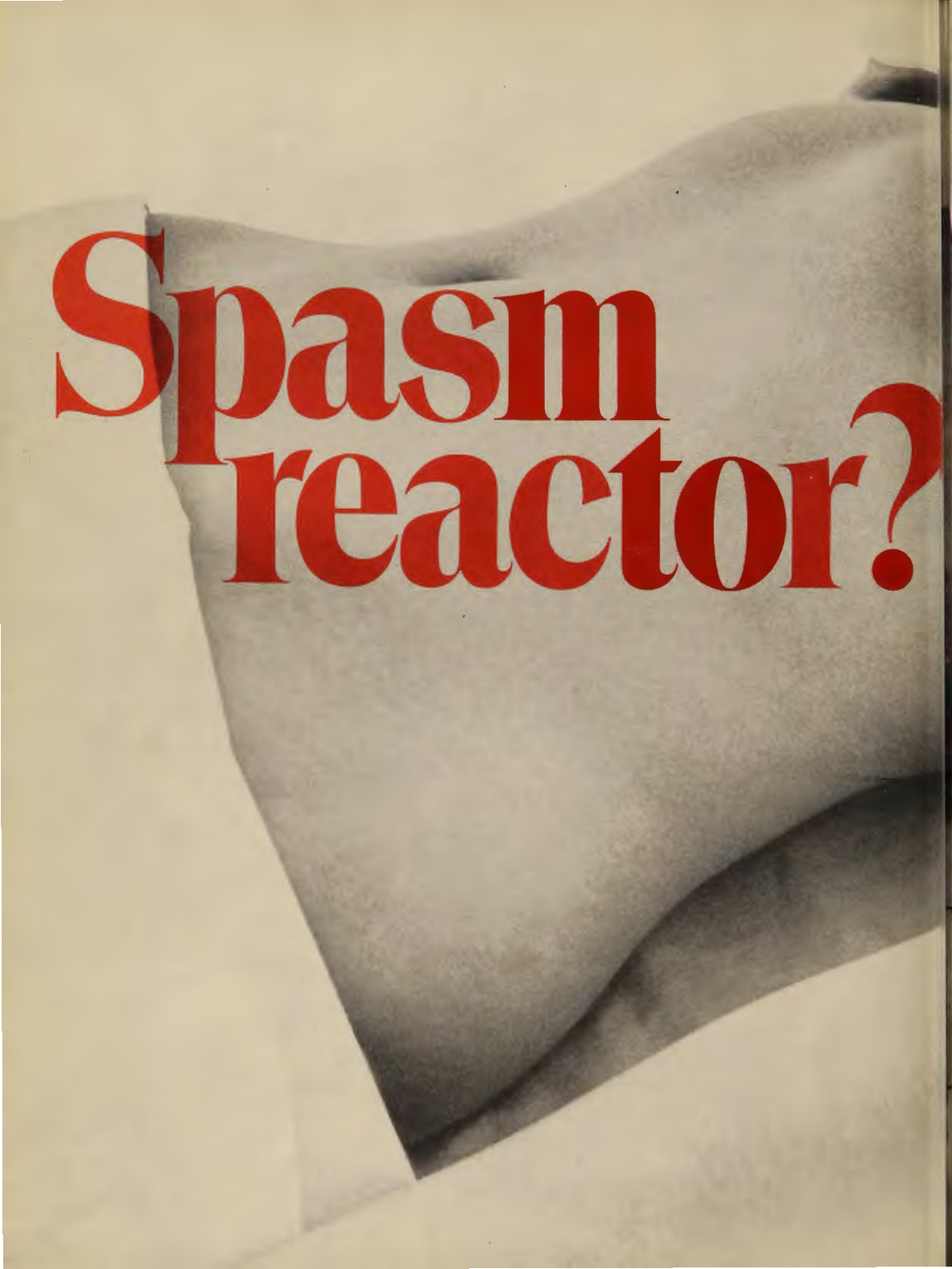
SYMPOSIUM ON ANESTHESIOLOGY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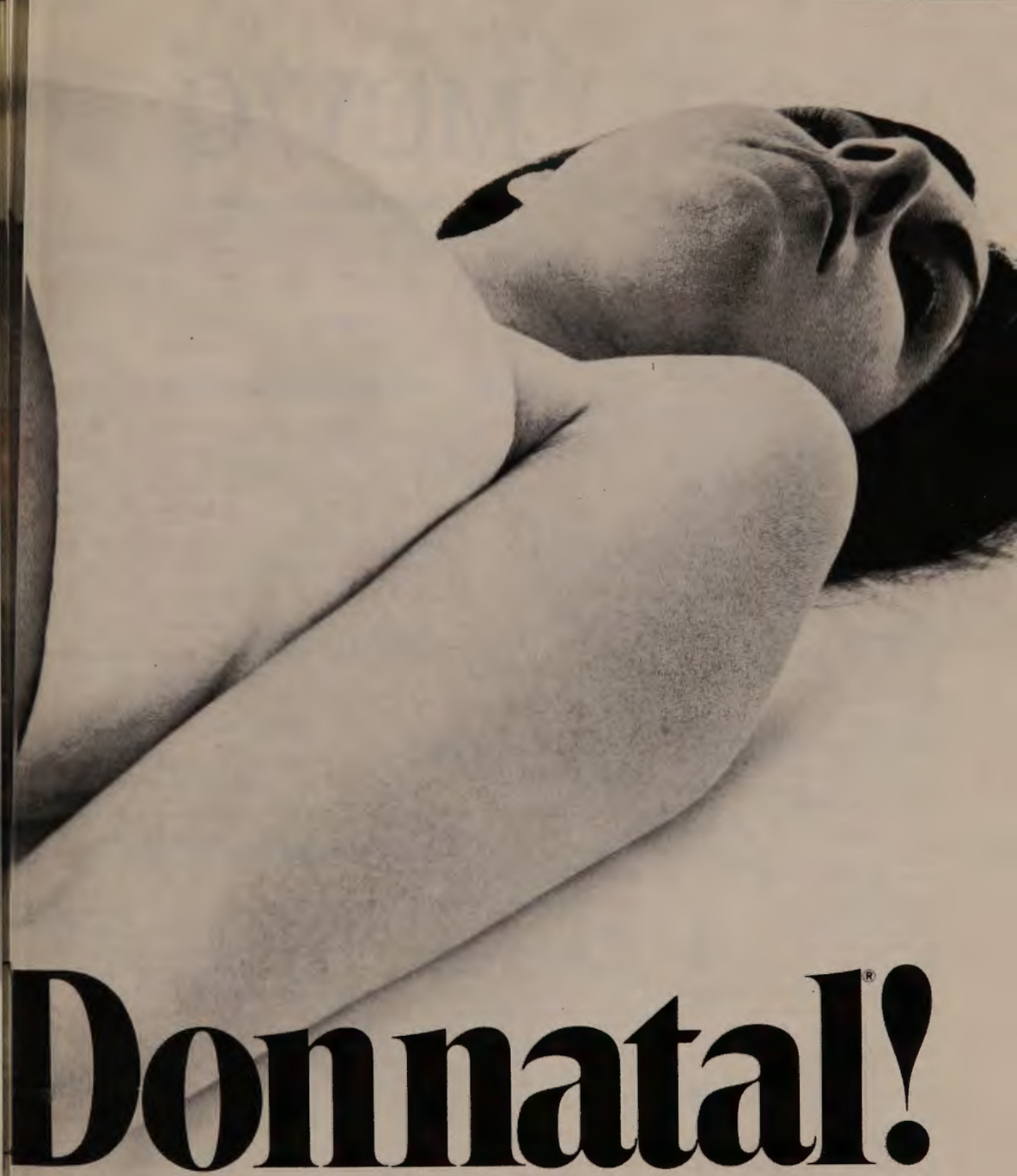

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atropine sulfate	0.0194 mg.	0.0194 mg.	0.0582 mg.
hyoscine hydrobromide	0.0065 mg.	0.0065 mg.	0.0195 mg.
phenobarbital	(¼ gr.) 16.2 mg.	(½ gr.) 32.4 mg.	(¾ gr.) 48.6 mg.

warning: may be habit forming

Brief summary. Side effects: Blurring of vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur on higher dosage levels, rarely on usual dosage. Administer with caution to patients with incipient glaucoma or urinary bladder neck obstruction as in prostatic hypertrophy. Contraindicated in patients with acute glaucoma, advanced renal or hepatic disease or a hypersensitivity to any of the ingredients.

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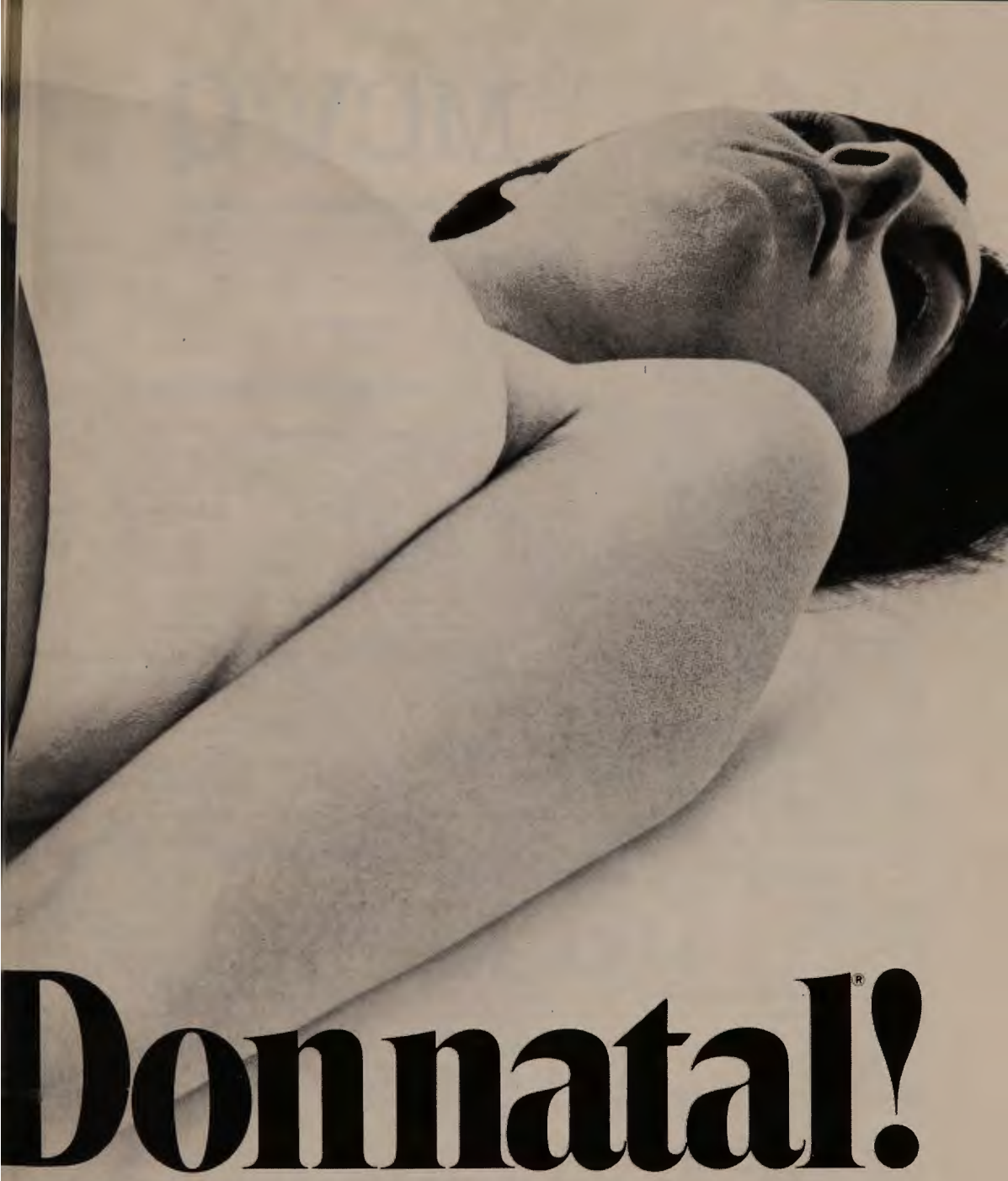

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CONTENTS

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What Is New in Anesthesiology?

The 25th Annual Stoneburner Lecture Series, held at the Medical College of Virginia, February 25-26, 1972, was devoted, for the first time since its inception in 1946, to Anesthesiology. Nineteen outstanding speakers from various parts of the country covered a wide range of pertinent subjects.

Anesthesiology is a relatively new medical specialty and is expanding rapidly. Guided by the dictum "primum non nocere," the modern anesthesiologist has to evaluate thoroughly any new anesthetics or techniques before accepting them as the best and the safest. The Stoneburner Lecturer, Dr. C. Ronald Stephen, Mallinckrodt Professor of Anesthesiology, gave an in-depth description of the 1972 trends in anesthesia and made predictions for the future.

I would like to extend my thanks to the Department of Visual Education of the Medical College of Virginia, which under the able guidance of Mr. Melvin Shafer, did an excellent job of taping the lectures and providing television coverage; to Dr. M. Pinson Neal, Jr. and Miss Erma L. Blanchard from the Department of Continuing Education; to other members of the Department of Anesthesiology who gave freely of their expertise and time to make the 1972 Stoneburner Lecture Series an outstanding success; and to the editorial staff of the MCV QUARTERLY who worked hard to edit this impressive issue containing most of the lectures presented at the symposium.

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Proper Use of Ketamine and Innovar*

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KETAMINE. Success or failure with the use of ketamine depends largely on three factors:

1. Awareness that ketamine is *different* from traditional anesthetics. These differences include the following:

   Ketamine, unlike traditional anesthetics which cause *total* depression of the central nervous system, affects *selectively* pain conduction and perception systems, stimulating one area of the brain while simultaneously depressing another ("dissociation").

   Ketamine *stimulates the cardiovascular system* while traditional anesthetics depress cardiovascular function.

   Ketamine has *antiarrhythmic* properties while traditional anesthetics do not. They may even precipitate arrhythmias.

   Ketamine maintains or even exaggerates *protective reflexes* while traditional anesthetics suppress them.

   Ketamine *ensures airway patency*, provided no mechanical airway obstruction is present, while traditional anesthetics require additional tools and techniques.

   Ketamine does not produce the traditional "anesthetized" appearance in the patient, but rather a characteristic *"disconnected"* appearance.

2. Knowledge of the criteria used for selection of patients for ketamine anesthesia:

   Use of ketamine predominantly in *infants* and *children* up to 14 years of age.

   The use of ketamine in adult patients is confined to surgical conditions for which ketamine has proven to be particularly advantageous, safe, and superior to conventional anesthetic agents and methods (see under 3).

   Narcotic addicts and patients with a history of chronic alcohol abuse or suffering from acute alcohol intoxication are poor candidates for ketamine anesthesia because in these patients even excessive doses of ketamine may fail to control body movements.

3. Limiting the use of ketamine anesthesia to the following specific *surgical areas and conditions:*

   Surgical treatment of burns*

   Neurodiagnostic procedures such as pneumoencephalography, ventriculography, myelography, and carotid arteriography.

   Out-patient ophthalmology (tonometry, fundoscopy, gonioscopy).

   Out-patient oral surgery (tooth extraction, surgery on the gingiva).

   Out-patient otology (myringotomy, insertion of myringeal tubes, removal of foreign body from ear canal).

   Out-patient plastic surgery (removal of nevi, suturing of laceration, removal of scars).

* Patients of all ages may be included.

* Presented at the 25th Annual Stoneburner Lecture Series, February 25, 1972, at the Medical College of Virginia, Richmond.

Elective orthopedic surgery (reduction of congenital hip luxation, spicacast application).
Emergency orthopedic surgery (closed reduction of fractures).

Repeated manipulation under anesthesia (irradiation of inoperable intraocular or intracranial lesions).

Induction of anesthesia in high-risk patients, including asthmatics, prior to the use of the principle anesthetic. Ketamine-induced cardiovascular stimulation and its relaxant effect on bronchial musculature offer significant advantages over conventional anesthetic agents.*

Cardiac catheterization.

Open heart surgery, particularly involving patients with minimal or no cardiac reserve. Cardiovascular stimulation and antiarrhythmic affects of ketamine offer prime advantages over traditional anesthetics.*

Emergency surgery in patients suffering from hypovolemia or shock-like conditions. Ketamine may be used for induction or to enhance minimal conventional anesthesia. It offers the advantage of ensuring cardiovascular support until conventional measures to control hypovolemia and shock can be instituted and become effective.*

Contraindications. Ketamine is contraindicated with hypertension, history of cerebrovascular accident, upper respiratory infection, increased cerebrospinal fluid pressure, abdominal surgery, and other surgery involving visceral pain (unless supplemented with conventional anesthetics).

Technique of Administration of Ketamine.

Pre-anesthetic medication: Infants and children receive scopolamine 0.1 to 0.4 mg, depending on age and weight, given intramuscularly ½ to 1 hour prior to surgery to counteract ketamine-induced hypersalivation. Pentobarbital or secobarbital (0.5 to 1 mg per pound) may be given for additional sedation.

Adult patients receive a tranquilizer with antipsychotic properties, preferably droperidol (1 to 2 ml) or Innovar® (1 to 2 ml) combined with 0.4 mg of atropine administered intramuscularly ½ to 1 hour prior to surgery. Other combinations of narcotic analgesics, tranquilizers, and ataractics have proven less effective as compared with the above-mentioned medication.

Omitting narcotics or barbiturates in the pre-anesthetic medication will significantly shorten recovery time. No pre-anesthetic medication is given to patients undergoing ambulatory surgery provided that the surgical procedure is limited to 15 minutes.

Induction: With the intravenous route, the initial dose of ketamine ranges from 1 to 2 mg per kg depending on the physical state of the patient. It is recommended that ketamine be administered slowly, over a period of 30 to 60 seconds. More rapid administration may result in respiratory depression.

With the intramuscular route, the initial dose of ketamine ranges from 6 to 12 mg per kg.

Maintenance: Supplemental increments of ½ to ⅓ of the full induction dose may be administered intravenously every 8 to 10 minutes or intramuscularly every 20 to 30 minutes, or when movements of head or extremities indicate lightening of anesthesia.

Complications. The following complications may be encountered:

Temporary *augmentation of pulse rate and blood pressure* beginning shortly after injection of the drug. This cardiovascular-stimulating effect of ketamine may prove beneficial in certain circumstances, for example, in the presence of hypotension or shock-like states. In hypertensive individuals, however, stimulation may be considered undesirable or unsafe.

Transient *depression of respiration* in response to rapid intravenous injection or in connection with an overdose of ketamine.

Paroxysmal coughing in the presence of upper respiratory infection, occurring immediately following the initial injection of ketamine and recurring with supplemental increments.

Vivid dreaming, with or without *psychomotor activity,* confusion, and irrational behavior occurring during emergence from anesthesia. This complication is more often observed in adults than in children and infants.

Tonic and clonic muscle movements resembling convulsive seizures occurring in certain patients without electroencephalographic evidence of seizure activity.

Erythema or morbilliform rash occurring subsequent to the initial injection of ketamine. The skin eruption is transient and usually confined to face, neck, and upper chest.

Treatment of Complications. Proper pre-anesthetic medication as outlined above may signficantly suppress or even eliminate most adverse reactions. This holds particularly true with regard to post-anesthetic emergence delirium reactions. The incidence and degree of these psychic disturbances can be further minimized by avoiding premature verbal or tactile stimulation of the patient ("sensory deprivation").

Post-anesthetic emergence delirium reactions, should they occur in spite of proper pre-anesthetic medication, may be successfully treated with intravenous droperidol—1 to 2 ml. Also recommended are ultra short-acting barbiturates such as pentothal or surital administered intravenously at doses of 75 to 100 mg.

Tonic and clonic movements during anesthesia may be effectively treated with small intravenous doses (2 to 5 mg) of diazepam (Valium®).

Ketamine does not provide adequate control of pain originating from the viscera. Therefore, the drug is not recommended for use as a sole anesthetic in abdominal or thoracic surgery or where visceral pain is expected to occur. In order to control visceral pain, ketamine may be supplemented with other general anesthetic agents.

In summary, ketamine, a phencyclidine derivative, is a unique and unusually safe, effective anesthetic agent. It is short-acting; it can be given either intravenously or intramuscularly; it is relatively easy to control, requiring little in the way of adjunctive or supportive drugs or devices. It differs markedly from previously established general anesthetics because of its selectivity with respect to the central nervous system. Ketamine is capable of simultaneously depressing cortico-thalamic pathways and activating limbic areas, referred to as "dissociation," and the resulting state is, therefore, termed "dissociative" anesthesia.

Profound analgesia is produced without concomitant respiratory depression and without inhibiting reflexes that protect the air passages. The cardiovascular system is slightly stimulated.

Ketamine has proved to be of unique value in the anesthetic management of patients, particularly infants and children, undergoing a variety of surgical and diagnostic procedures involving the head, neck, and extremities and those necessitating frequent position changes such as are encountered in neurosurgical diagnostic procedures and in the treatment of severely burned patients of any age.

Properly administered and with due regard for its specific advantages as well as its possible disadvantages, ketamine may prove superior to conventional anesthetic agents and methods in a variety of specific surgical procedures.

INNOVAR. Innovar is a mixture of two drugs: *droperidol,* a butyrophenone derivative, with strong tranquilizing, antiemetic, and adrenergic-blocking properties; and *fentanyl,* a powerful narcotic analgesic related to meperidine which differs from conventional narcotics by its high potency and its fast onset and short duration of action. The two drugs are mixed in a ratio of 50 to 1. When administered intravenously in appropriate doses, a state of neurolept*analgesia* is produced in which the patient is rendered immobile and insensitive to pain. His face being expressionless, the patient appears detached from his surroundings, yet he remains alert and cooperative. Respiratory function is depressed and it may be necessary to assist or control the respiration via a face mask or endotracheal tube. If nitrous oxide-oxygen mixtures are added to produce sleep and memory deficit, the state of neurolept*anesthesia* is established.

Innovar or its separate component drugs, droperidol and fentanyl, can and will provide optimal conditions for the patient and surgeon provided that *certain basic principles and rules are observed* along with the use of the drugs which may be listed as follows:

1. Adherence to minute details with regard to the *technique* of administering the neuroleptanalgesic drugs.
2. Employing neuroleptanalgesia and anesthesia preferably in *poor-risk, debilitated, or geriatric patients* undergoing *major, traumatic, and prolonged surgery,* and avoiding their use in pediatric surgery and in short-lasting, uncomplicated, and minor surgery.

Technique of Administration of Innovar or Its Separate Components, Droperidol and Fentanyl, to Produce Neuroleptanalgesia.

Pre-anesthetic medication: Droperidol alone (2.5 to 10 mg, depending on age and physical state) or Innovar (1 to 2 ml) is given intramuscularly 30 to 60 minutes prior to surgery. Atropine or scopolamine (0.4 to 0.6 mg i.m.) may be added to control secretions.

Induction using Innovar: The recommended dose of Innovar is 1.0 ml per 25 pounds of body weight. This may be reduced to 0.5 ml per 25 pounds

of body weight in extremely poor-risk and debilitated patients. Individuals in good physical state may receive 1.5 to 2.0 ml per 25 pounds of body weight. In a patient of average weight the total calculated dose of Innovar ranges from 6 to 8 ml. Debilitated and reduced patients may receive 5, 4, or 3 ml, while patients in a satisfactory physical state may receive 9 or 10 ml. The total dose of Innovar will rarely exceed 10 ml.

A *test dose of 1 to 2 ml* of Innovar injected intravenously over a period of 1 minute is *always* used prior to the administration of the full calculated dose. One to two minutes following the injection of the test dose, the blood pressure is recorded, and if unchanged, the remainder of the dose is administered. A *blood pressure drop* of more than 25 mm Hg in response to the intravenous test dose usually indicates inadequate circulatory volume requiring *rapid intravenous infusion* of 500 to 1,000 mm of fluids before proceeding with further administration of Innovar.

The compounded total dose of Innovar may be administered as follows:

a. *Intravenous drip:* The solution to be infused should contain 10 ml of Innovar added to 250 ml of 5% dextrose in water or saline. This mixture is administered by the microdrip technique at the rate of 150 to 200 drops per minute. When increased somnolence and psychic detachment are noticeable —usually within 3 to 5 minutes after start of the infusion—a local anesthetic (cocaine 5%, lidocaine 4%) is topically applied either by intralaryngeal spray or by injection through the crico-thyroid membrane. When the patient's respiratory rate has slowed to 10 per minute, the intravenous drip is slowed to 100 drops per minute. At this point, psychic indifference is further enhanced, and analgesia has usually reached the optimal level. The intravenous drip is then discontinued and the patient is ready for the surgical procedure while still responding to commands such as "take a deep breath" or "open your mouth."

b. *Intravenous injection:* The calculated dose of Innovar is injected intravenously in increments of 1.0 to 2.0 ml over a period of two to three minutes.

Maintenance: In order to hold the level of surgical analgesia, *fentanyl* in doses of 0.05 to 0.1 mg (1 to 2 ml) is administered intravenously when changes in vital signs such as increased heart rate, elevated blood pressure, increased respiratory rate, or irregular breathing indicate lowering of the pain threshold. It is *not* recommended that *Innovar* be administered for maintenance of surgical analgesia because of possible cumulative effects of the longer-acting droperidol which may result in over-tranquilization postoperatively.

Postoperative period: Usually, analgesia extends well into the postoperative period. Therefore, patients rarely require narcotic analgesics for pain relief. If narcotic analgesics are administered, their dose should be reduced to ¼ or ⅓ of the usually recommended dose.

Induction using droperidol and fentanyl as separate drugs: Induction is started with the intravenous administration of droperidol (0.15 mg per kg). The patient's vital signs are observed for 5 to 6 minutes and if no change is noted, an initial dose of 20 to 60 mcg of fentanyl is administered intravenously followed by 20 to 40 mcg doses of fentanyl, given at about two-minute intervals at which time the patient is considered ready for the operative procedure.

Indications. Neuroleptanalgesia should be limited to patients in whom *retention of consciousness* and *cooperation* during the surgical procedure is desired. Such procedures include: bronchoscopy, laryngoscopy, and esophagoscopy; neurodiagnostic procedures such as pneumoencephalography and carotid arteriography; cardiac catheterization; stereotactic procedures including cryothalamotomy; resection of epileptogenic focus; ophthalmic surgery (in conjunction with regional anesthesia); middle and inner ear surgery (in conjunction with local anesthesia); and oral surgery including tooth extraction and other intraoral surgical procedures involving the gingiva and the tongue.

Contraindications. Neuroleptanalgesia is contraindicated for ambulatory surgery, surgery in infants and children, acute alcohol delirium or history of alcoholism, and narcotic addicts.

Technique of Administration of Innovar or Its Separate Components, Droperidol and Fentanyl, to Produce Neuroleptanesthesia.

Pre-anesthetic medication: This is the same as that described under neuroleptanalgesia as is the composition of the total dose to be administered for producing the neuroleptanesthetic state.

Induction: Innovar may be administered as follows:

a. *Intravenous drip:* Preparation of the solution to be infused and induction are identical with the method described under neurolept*analgesia*. At the time the patient shows signs of somnolence and obtundation in response to the infusion, the intravenous drip is slowed to 100 drops per minute and continued at this rate throughout the anesthesia course. Administration of nitrous oxide-oxygen (4:2) by face mask is begun, and the patient is encouraged to take deep breaths. Within one minute the patient usually lapses into unconsciousness without excitement. An intravenous dose of short-acting muscle relaxant is administered to facilitate endotracheal intubation and to counteract muscle rigidity which may develop during this phase. As a rule, the patient resumes spontaneous breathing within five to eight minutes. D-tubocurarine is administered intravenously at conventional dosages if muscle relaxation is needed for surgery. When changes in vital signs indicate lightening of anesthesia, the drip rate is increased until vital signs return to normal.

b. *Intravenous injection:* Similar to the method of neuroleptanalgesia, a test dose of 1 to 2 ml of Innovar is administered intravenously over a period of 1 minute. Blood pressure is recorded subsequent to this injection and, if found essentially unchanged, further increments of 1 to 2 ml of Innovar are administered intravenously at 1- to 2-minute intervals. By the time the total calculated dose has been administered, the patient shows signs of drowsiness and increasing tranquilization. While the patient still is able to respond to questioning, the breathing mask is applied and nitrous oxide-oxygen, at the flow of 4 liters of nitrous oxide and 2 liters of oxygen per minute, is administered. While spontaneous breathing is increasingly more depressed, positive pressure ventilation via the face mask is begun with the patient responding to the command to take deep breaths. As a rule, after 5 to 8 breaths the patient lapses into unconsciousness without excitement. Immediately prior to the loss of consciousness, an intravenous dose of a short-acting muscle relaxant is administered to facilitate endotracheal intubation and avoid the development of fentanyl-induced muscle rigidity.

Maintenance: For maintenance of the neuroleptanesthetic state, administration of nitrous oxide-oxygen (4:2) is continued. Fentanyl is administered intravenously at doses to 1 to 2 ml (0.05 to 0.1 mg) when changes in vital signs (increased heart rate, elevated blood pressure, increased respiratory rate, or irregular breathing) indicate lowering of the pain threshold. The response to the administration of fentanyl is usually prompt, and signs of inadequate pain threshold elevation disappear within 45 to 60 seconds. If the vital signs continue to indicate insufficient analgesia, another increment of 1 to 2 ml of fentanyl is administered intravenously. In an average patient, administration of supplemental intravenous fentanyl doses is required at 45 to 60 minute intervals. Fentanyl for maintenance of anesthesia may also be given intramuscularly at the same dose as mentioned above. Adequate pain threshold elevation usually is accomplished with this route of administration within 7 to 8 minutes and may last up to 2 hours.

In abdominal surgery or other procedures requiring muscle relaxation, d-tubocurarine may be administered at conventional intravenous doses.

Emergence: Return to consciousness is rapid, as soon as the administration of nitrous oxide-oxygen is discontinued. Within 3 to 5 minutes the patient is usually in contact and can answer questions. If respiratory exchange is inadequate, the endotracheal tube may be left in place in order to mechanically support ventilation until satisfactory respiratory function is reestablished, at which time the endotracheal tube is removed. Levallorphan (Lorfan®) may also be given at intravenous doses of 1 mg to counteract fentanyl-induced respiratory depression. If Lorfan fails to restore adequate respiratory function, other factors causing respiratory depression should be examined.

Complete analgesia usually is maintained for 4 to 6 hours. Nausea and vomiting are rarely encountered.

Indications. Neuroleptanesthesia is indicated for the following: biliary surgery for which halogenated anesthetics may be contraindicated; major, traumatic, prolonged surgery involving poor-risk patients; neurosurgery; cardiovascular surgery including open heart procedures; surgery for organ transplantation, particularly kidney transplants; middle and inner ear surgery; and emergency surgery involving elderly, debilitated, and reduced patients; and patients in shock-like states.

Contraindications. The contraindications for neuroleptanesthesia are the same as those under neuroleptanalgesia. In addition, the use of Innovar may be contraindicated in asthmatic patients since it may precipitate an attack.

Complications. *Hypotension* is most commonly

encountered during induction of neuroleptanesthesia, indicating inadequate circulatory volume and inability of the patient to compensate for peripheral vasodilatation caused by droperidol-induced alpha-adrenergic blockade. Treatment should consist of rapid infusion of 500 to 1,000 ml of lactated Ringer's solution or 5% dextrose in water solution in preference of the use of vasopressors.

Excessive blood pressure elevation, the etiology of which is undetermined, has occurred in rare instances. Intermittent administration of halothane at conventional concentrations or small intravenous doses of chlorpromazine (7.5 to 15 mg i.v.) have proved to be effective in restoring acceptable blood pressure levels.

Droperidol may induce *extrapyramidal muscle activity* which may be controlled with anti-Parkinson agents such as Cogentin®.

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How Safe is Halothane?*

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Halothane (2-bromo-2-chloro-1, 1, 1-trifluoroethane) is the most popular inhalation agent in today's anesthetic practice. Its desirable properties include high potency, nonflammability, patient acceptance, a low incidence of nausea and vomiting, ability to produce bronchodilatation, and ease of maintenance. Prior to its introduction in 1956, it was subjected to an intense examination for both general and hepatic toxicity. Although these investigations disclosed no evidence of adverse effects, reports of liver dysfunction after halothane administration have appeared constantly in the literature. Thus, although the general safety of this drug continues to be excellent, the clinician is confronted with a dilemma each time he elects to use this agent. I hope to give some perspective to this question.

The first thing to understand is that administration of any of the anesthetics currently in use may be followed by mild and reversible evidence of liver derangement. Studies conducted over twenty years ago showed that administration of diethyl ether or cyclopropane was followed by significant bromsulfalein retention, a phenomenon also observed when spinal anesthesia was used. Subsequent investigations have shown this to be true in the case of methoxyflurane and halothane. Other work has indicated that clearance of indocyanine green (ICG) is markedly diminished during anesthesia. It would thus appear that all anesthetics have the ability to produce mild and reversible evidence of hepatic abnormalities; findings which are probably of no physiologic significance. This property is shared by halothane.

Halothane also produces reversible abnormalities of hepatic mitochondrial function. Oxygen uptake of mitochondria stimulated by adenosine diphosphate is diminished in the presence of clinically effective concentrations of halothane. Halothane, however, is no different from methoxyflurane, diethyl ether, and ethrane which also produce these changes. Thus, although halothane has specific metabolic effects, it shares these in common with other inhalation agents.

Perhaps halothane exerts its effects through altered hepatic circulation. Studies performed in man during halothane anesthesia indicate that splanchnic blood flow decreases as mean arterial pressure is lowered; ICG clearance is diminished also. However, when arterial carbon dioxide tension is elevated, splanchnic vasodilatation occurs and splanchnic blood flow is increased. In spite of the return of blood flow to normal, ICG clearance remains depressed. Cyclopropane, on the other hand, increases arterial pressure while hepatic blood flow is decreased. Again, ICG clearance is lowered. When hexamethonium is infused, splanchnic vascular resistance decreases and splanchnic flow is elevated. As in the case of halothane, the return of hepatic perfusion to normal does not result in a normal ICG clearance. Again, we must consider the abnormality in ICG clearance to be a nonspecific anesthetic effect rather than the pathologic manifestation of a low perfusion state. We must also realize that halothane does not have a specific effect, and that this phenomenon is observed with all the inhalation agents.

It is clear that the major question which must be answered for any anesthetic agent concerns its overall safety. It is because of this problem that a retrospective study of anesthetic safety during the years 1959-1963 was undertaken. This study, known as the National Halothane Study, evaluated the records of 865,515 anesthetics. In this group, 16,840 deaths were reported of which 11,289 underwent autopsy. There were two significant questions which

* Presented at the 25th Annual Stoneburner Lecture Series, February 25, 1972, at the Medical College of Virginia, Richmond.

were posed: (1) Were there differences among anesthetic agents and techniques in overall death rates and in the incidence of massive hepatic necrosis? (2) Were there any differences among anesthetic agents and techniques in the death rate or incidence of massive hepatic necrosis when surgery in the biliary tract was performed? The overall results of the study suggested that halothane was at least as safe as the other agents examined. Furthermore, it was no less safe than the other drugs when biliary surgery was performed.

Although the data suggested that halothane's safety was at least equal to that of other drugs and techniques, a certain nagging doubt persisted. Most of the cases of hepatic necrosis were obviously caused by factors such as hemorrhagic shock, sepsis, or previous transfusion. However, in nine cases no etiology was obvious and of these, seven had received halothane. Furthermore, four of these seven had been exposed previously to halothane. It must be realized that the National Halothane Study had an element of volunteer bias in that several of the unexplained cases of massive hepatic necrosis had already been published, and most probably the institution volunteered to participate in the study because of this. Nonetheless, the possibility was considered that halothane might be responsible for certain cases of hepatic dysfunction.

In subsequent years, a number of events were reported which indicated that exposure of unoperated man to extremely low concentrations of the agent might rarely produce hepatic abnormalities. It was from a consideration of such events that the concept of halothane hypersensitivity arose. This theory stated that halothane is not a direct hepatotoxin. In the rare cases (the incidence of unexplained hepatic necrosis following halothane was 1:35,000), the individual might be hypersensitive or "allergic" to the agent. This would explain the increased likelihood of observing the phenomenon after more than one exposure, and might also explain the occurrence in unoperated man receiving sub-anesthetic concentrations of the drug. Additional support to this theory was evidence of lymphocyte transformation produced by incubating lymphocytes of affected man with halothane. It should be noted that many individuals with what appears to be halothane-induced hepatitis did not show positive lymphocyte transformation. Furthermore, occasional false positive results have been reported. Thus, although the hypersensitivity theory is not unreasonable, it should not be considered to be the sole explanation of this unfortunate phenomenon.

We have recently studied the concentrations of immunoglobulins in man following surgery performed during halothane anesthesia. Observations were made prior to and up to 30 days after surgery; data obtained was compared with similar studies when anesthesia was provided by nitrous oxide supplemented with narcotic. No significant changes were produced by either nitrous oxide-narcotic or nitrous oxide-halothane. In another group of individuals receiving halothane anesthesia, measurements of serum glutamic oxaloacetic transaminase concentration and bromsulfalein retention accompanied the assays of immunoglobulin concentrations. Although transient abnormalities of hepatic function were observed, no alterations in the immunoglobulin pattern were noted during observations lasting as long as 60 days.

Although these data do not definitely rule out an immunologic basis for halothane-induced hepatic necrosis, they do suggest that a systematic immunologic abnormality does not occur usually following anesthesia with this agent. Furthermore, they indicate that short-lived abnormalities of hepatic function following halothane anesthesia are similar to those observed with other anesthetic drugs and are not the result of immunologic factors. Finally, these observations furnish a base line should the opportunity arise to obtain samples from a patient with severe hepatic failure following halothane anesthesia.

Are there any other mechanisms which might be responsible? In the past few years, increasing emphasis has been placed on the ability of the hepatic microsomal system to detoxify a wide variety of drugs. Many of the inhalation anesthetics, among them halothane, are so metabolized. Furthermore, prior exposure to halothane produces enzyme induction which results in a more rapid rate of halothane biodegradation. It is not inconceivable that abnormal pathways of biodegradation might produce toxic metabolites which could result in hepatic necrosis.

At the present time, the evidence is not clear as to what might be the mechanism for the extremely rare case of halothane-induced hepatic necrosis. Indeed, it is still a moot point as to whether this entity can be definitely proven to exist. However, the answer to the question of this lecture can be easily made. The National Halothane Study supplied excel-

lent data indicating that in the overwhelming majority of patients the drug is as safe as any currently used. I would suggest that the main factor determining patient safety is the individual administering the anesthetic rather than the specific agent itself. However, although the drug is exceedingly safe, a small number of patients may be at risk. It is the task of future investigation to delineate these individuals so as to prevent the occurrence of this syndrome.

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Health Care and the Anesthesiologist: Influence and Factors*

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When one asks me today what are the special factors that influence the health care delivery of anesthesiologists, I am compelled to say that they are almost identical with those factors which influence the delivery of health care for all physicians.

The first and major influence is the role of government. Probably the most beneficial impact of government activity in the past decade has been the advent of Medicare in June of 1966. This is an excellent program which has truly provided marked beneficial results for the elderly. It has brought more talented medical care to the aged at a minimum of cost and, up to now, at a reasonable reimbursement level. On the other hand, the Medicaid or Title 19 activity which was added to the Medicare legislation at the last moment has proven itself to be a colossal fraud. This was simply overpromising and underfunding. In many areas of the country, institutions and health care providers are underfunded to the extent that billing for services is not worthwhile. Hence, this large poor segment of the population is left with no better health care delivery than it had before the inception of the Medicaid proposition.

Attendant to the Medicare legislation was the establishment in each major health care institution of a utilization review committee which would study the effectiveness of medical care delivery of its practitioners. This was geared to increase productivity of overcrowded hospital facilities. In many areas this has proved extremely effective. Hospitalization periods have been reduced, many unnecessary costs have been limited, and hospital beds are more readily available so that there is a more efficient turnover of acute care patients. In this regard, one of the challenging problems affecting government and health professions in general is the accuracy of predicted demographic projections for the immediate and remote future. At present, our country of over 200,000,000 people has 11,000 anesthesiologists and some 15,000 nurse anesthetists delivering anesthesia care for some 15,000,000 major surgical procedures performed in this nation each year. Initial projections before the concern with population growth were that we should have a total population of some 275,000,000 people by 1985. With the recent changes in birth rate, it is projected that we shall not have such a population abundance until closer to the year 2000. This problem ties in very directly with the utilization efficiency of the numbers of anesthetists, both anesthesiologists and nurse anesthetists, that we now have in ratio to population and our concerns for projecting our adequate future supply. In both of these areas, manpower has been increasing adequately over the past decade. One thought has been to supply physicians' assistants in this area. There are several schools where physicians' assistants in anesthesia and job identification of anesthesiologists' functions are being developed. I cannot conceive that this is a universal need, for the physicians and nurse anesthetists are presently doing a most adequate job and have a depth and scope of information which leads to a more adequate judgment so necessary for quality patient care in the operating amphitheater. In a study of ten hospitals conducted by the American Society of Anesthesiologists in 1969 and repeated in 1970 with almost identical results, the surgical anesthesia committee of this society found that the operating room efficiency in terms of operating rooms utilized per man hour of anesthesiologists and anesthetists available and per eight-hour working day was somewhat below 50%. Efficiency seemed to increase

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with the increase in hospital size, and where a teaching setting was involved. In such institutions the mode curve ran as high as 55 to 60%. It stands to reason, therefore, that with our present numbers we can simply double our efficiency and effective delivery of health care by a more careful scheduling of operative procedures. The anesthesiologist has extended his arm outside of the operating room, particularly in intensive care, emergency care, and coronary care facilities. It is here that his special talents have proved so successful. It is here also that the immediate continued attention of the anesthesiologist is not necessary in the same degree or in the same manner as it is necessary in the operating room. It is here, therefore, that I believe a physician's assistant in anesthesiology will be a very effective mechanism for improvement of anesthesia care in general. Studies in the effective utilization of operating rooms and demographic projections of manpower within the speciality are presently being continued under the auspices of the American Society of Anesthesiologists.

"Peer review" is something everyone seems to be talking about. There does not seem to be a consensus of application with the exception that everyone understands it is a quality analysis of the effectiveness of the health professional, both in terms of the capacity of his professional competence and his socio-economic delivery. Needless to say, any regulation of the quality of the professional activity of physicians and other professionals can only be effectively established by those professionals themselves. No lay government bureaucrat can expect to succeed in this area. They have neither the knowledge nor the know-how.

One of the most recent influences in health care delivery that is affecting the government, the patients, and the anesthesiologists as well as physicians in general is the mounting cost of malpractice. When I started in medical practice some twenty-odd-years ago, my premiums for $100,000-$300,000 malpractice coverage were $102.00 per year. Today, in New York, a policy with $2,000,000-$6,000,000 coverage, which is necessary because of the frequency and increasing fees of malpractice defense, is $6,000 per year. This has been one of the most troublesome areas in rising costs of medical delivery by professionals. The professional cannot be expected to absorb all of this expense, and a great deal of it has been passed on to the patient as evidenced by increasing fees. Malpractice coverage costs have also increased health costs in general by creating the need for more expensive laboratory tests and by limiting a certain professional therapeutic activity to very costly methods where there is a high degree of safety. At present, there is a presidential commission studying this problem. All we can say is that we urge their haste before malpractice premiums raise the rate of health care delivery beyond any reasonable expectation.

There has been a recent surge toward prepaid clinic development. This is taking several different directions. Basically we are talking of that which is known as health maintenance organizations. These may be institutional and they may be individual. The Department of Health, Education, and Welfare over the past year has been actively involved in the development and planning of such HMO's on a pilot basis. Needless to say, of the eleven functioning at this time all are in serious financial straits, with one exception, and a much more extensive review of this HMO problem and projection of financial operation must be undertaken before any reliable results might be expected.

The second major influencing factor in health care delivery in the United States is the activity of the American Medical Association. I think it is important to say that there has been a great swing in the philosophy of activity within this organization, particularly regarding scientific and educational opportunities. This has been all for the good. The most interesting of the changes is in the fact that as of July of this year, the specialty organizations within medicine will take over most of the responsibility for scientific programming at annual and clinical meetings of the AMA.

There also has been an extension of the lines of communication within the AMA between the medical specialties and the officers, trustees and delegates. The first of these has been the development of the Section Councils which will be chosen for the most part by the parent specialty organizations. It is these Section Councils that will augment, authorize, and be responsible for the scientific activities presented as educational efforts of the AMA. The second line of communication has been the development of the Interspecialty Committee of the AMA's Board of Trustees so that specialties now have direct representation and voice channeled to the trustees of the organization. This provides for a rapid, informed dialogue between both organizations involved and the specialties at large.

Another important change in the American Medical Association has been the activity of its Council on Education. The Council has been instrumental in implementing the thinking published in the Millis Report. As you all know, internships are being phased out. There is an attempt to shorten the medical curriculum. In this regard, the AMA, the American Hospital Association, The American Association of Medical Colleges, The American Medical Specialty Boards, and the Council of Medical Specialties Societies are in the process of agreeing on a projected development of liaison committees for undergraduate and postgraduate medical education. There is no doubt that their thinking will eventually extend to Continuing Education and to Allied Health Professionals with the development of liaison committees in each of these groups together with representation from each of the parent organizing groups. Overseeing all of this will be a coordinating council which will have representation from each of the liaison committees and will be responsible as a single voice for medicine to the United States Commissioner of Education. This will probably prove to be one of the most effective links American medicine has ever had for a productive coordinated delivery. Of course, it is important at this time to realize that the early locking-in of a young medical specialist, whether he be in one of the surgical, medical, or family practice specialties, may influence the ability of future graduates in medicine and postgraduate training in their ability to pass present medical examinations. They may not easily swing from one medical specialty to another with the same freedom of license to practice medicine. Consequently, there are many areas now where it is thought that an M.D. degree might eventually have to be modified so that it would specify a particular parameter of activity such as a medical specialty. Hence, in the future one might see M.D. (Anesthesiology) or M.D. (Surgery). This will also probably call for a complete change in licensing examinations on a nationwide basis unless there is a very adequate and broad depth of medical information funded to a young medical graduate with a foreshortened curriculum who is locked into a particular specialty early in his medical existence.

The third major influence on health care delivery of anesthesiology is the American Society of Anesthesiologists. This is a national federation of twenty-four component societies. It is extremely effective organizationally as a unifying force for education, for combined efforts, and for the production of standards within the specialty. The ASA is also a very effective liaison organization with the other specialties of medicine and with government where it speaks with one voice. It has just adopted a requirement for Continuing Education for continued membership.

In summary, then, let us say that there are many factors influencing health care delivery of anesthesia in the United States. The people of this country expect improved delivery of medical care. The medical profession stands ready to do its part. And it expects the government to assume its liability. Simply stated, that means adequate funding.

The Anesthesiologist-Anesthetist Team*

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How ironic it is that we should be presenting the team concept of anesthesia practice at a conference whose format is "What Is New in Anesthesiology." Ironic because the team concept is not new in medicine in 1972. It has evolved in many areas with outstanding success in all. For example: coronary care units could not function so efficiently and excellently without teamwork; patients requiring acute and chronic respiratory care would probably be doomed without a team of physicians, nurses, and technicians; and stroke victims requiring the expertise of the physician during the acute phase of their illness, could not realize their full potential once again without a team of nurses, speech therapists, physical therapists, and other Allied Health Professionals. So also in anesthesiology, the concept of a team of anesthetists and anesthesiologists must evolve to enable us to adequately meet the needs of our consumer—the patient.

Let us for a moment digress and think about the patient, after all he is the reason why we do what we do. Have you noticed how sophisticated he has become lately? Insurance companies certainly have. No longer are we afforded the luxury of mysticism in medical practice. Medical knowledge, little as it may be, is possessed by a significantly greater segment of the population than ever before. The patient now demands his money's worth from the high cost of medical care. Magazines and newspapers, such as the Wall Street Journal, with their tremendous circulations make sensational headlines about the occasionally disastrous, albeit rare, effects of drugs or therapy. When reading such information, the patient more often than not becomes actually more misinformed than informed. Nevertheless, he takes this information (or misinformation) to the hospital with him practically demanding that we guarantee him safe passage through his illness.

Anesthesiology has by no means been able to escape the well-informed patient. In fact, it seems to me that as a specialty we have been practically singled out by the intellectual patient and his attorney. With the increasing onslaught of medical pseudo-education available to the consumer and our lack of ability or desire to set the record straight for him, our clinical judgment in many instances is in jeopardy of being compromised by our legal judgment. Because of the more sophisticated consumer and the trend towards team medicine in general, it is absolutely essential that where physicians and nurses work together to deliver this health care service they do so as a team.

Unfortunately, the team concept is not commonplace in anesthesia today. This situation prevails because relations between the anesthesiologist and the anesthetist have not been good over the years. Anesthesiologists have claimed that they should be the only professionals to deliver this type of health care; nurse anesthetists have made similar claims. Anesthesiologists have not enjoyed the prestige that their colleagues in surgery or other specialties have received. After all, what self-respecting doctor would want to devote his professional life to the same task that could be performed just as well by a nurse? On the other hand, nurses have not enjoyed the greatest acceptance into the specialty by their colleagues who, to this day, do not consider schools of anesthesia as offering post-graduate nursing education. Animosity and bad relations have through the years been the rule rather than the exception between CRNA's and M.D.'s. In many local areas today, nurse anesthetists feel threatened

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by the presence of anesthesiologists and vice versa. We cannot deny that in some areas there is good reason for these feelings to exist. Unethical practices on the part of both groups have not served any beneficial purposes except those of the practitioners.

In 1970, the American Society of Anesthesiologists invited several nurse anesthetist educators to participate in a symposium conducted at the annual meeting. I was honored to have been the first speaker on that program, and at that time I saw great hope for the future interrelations of our respective groups. My view has not changed in 1972. Recent steps taken by both the American Association of Nurse Anesthetists and the American Society of Anesthesiologists to assure better relations between the two have convinced me that a team of well-trained nurse anesthetists and anesthesiologists is the single best answer to the challenges the future will bring.

The trend toward development of programs to train nonprofessional anesthesia technicians to supply manpower in this health care area is in my opinion an unnecessary endeavor and a mistake. There is no shortage of applicants to our program for nurse anesthetists, and I am sure this situation exists in most other schools as well. There is, however, a limit to available space in all schools, and this will probably continue as long as the teacher shortage exists and until more facilities are constructed. The establishment of technical programs to educate assistants whose functions are limited, backgrounds diverse, motivation uncertain, and whose place is still ill-defined is beyond my comprehension.

Anesthesiology is the one speciality which has had for years physicians' ideal assistants but has failed to utilize them. Nurse anesthetist programs have evolved to high degrees of excellence through the efforts of many talented individuals, and the full potential of these programs is still to be realized. The awarding of an academic degree in conjunction with professional certification is now a reality. This trend must and will continue. University officials are now beginning to recognize their obligation to educate as well as train nurse anesthetists so that they may not only be prepared for clinical practice, but also be qualified by degree to teach others in the field. In short, the nurse anesthetist and anesthesiologist learning together and practicing together are the future of anesthesia health care delivery in this country.

How is such a team to be suddenly implemented after years of indifference? The answer is both complex and simple. It requires maturity and a realization of limitations, capabilities, and potential of all members of the group.

Just as a football team requires a quarterback to call signals and make plays, so the anesthesia team requires a leader. The quarterback of the anesthesia team is acknowledged to be the physician; however, without lineman for defense and pass receivers to carry the ball, the quarterback would not get very far before being inundated by the opposing line. In our anesthesia team, the nurse anesthetist backfield often carries the ball. Nevertheless, we must never forget that in all successful football teams the quarterback has been not only a playmaker, but also a scrambler who is capable and willing to take the ball downfield himself.

The Anesthesiologist. An important part of residency training, it would seem to me, should be spent in learning how to supervise. This is the most neglected phase of resident teaching, but its importance must not be underestimated. All too often the anesthesiologist finds himself in a situation where he is responsible for two or three operating rooms at one time. If he has experienced this during his residency, he will be much better prepared to act as the consultant and overseer of the anesthetists who are actually administering the anesthetics. I submit that it is much more difficult to supervise two or three anesthetic administrations than to be responsible for the actual administration of only one.

If the anesthesiologist is to be an effective supervisor, he must be an accomplished clinician. Currently, most residencies offer an abundance of clinical experience, thereby meeting this requirement. The anesthesiologist must know the problems of the individual patients whose anesthetics he is supervising. This knowledge can be gained during the preoperative visits. He must be able to identify which of these patients is most likely to require the closest attention. Finally, he must know the limitations and capabilities of the individual anesthetist assigned to administer the anesthetics. This all-important knowledge will enable him to provide all of the patients with the best possible care available.

Teaching the resident to supervise would be best accomplished in the latter part of the final year of a two- or three-year residency. At this time, the clinical experience should be adequate and the knowledge of individual capabilities should be known.

It would probably be best to assign the resident supervisor to cases which would be performed by experienced staff members rather than other students or residents in the department. Experienced staff members are generally more mature, and rapport with them can be established more easily than with students who may not readily accept supervision by someone other than the clinical instructors and attending physicians with whom they are accustomed to working. Also, the beginning supervisor should not have the added burden of working with inexperienced persons while he himself is learning. In my opinion, teaching proper clinical supervision to residents is a necessary part of anesthesia education and a must if the team concept of anesthesia care is to be successful.

The Nurse Anesthetist. With the organization of colleges of Allied Health Professions, nurse anesthetist programs have finally found a place where they can grow and develop independently, yet in conjunction with the university. A program based in Allied Health can offer students the benefits of university level basic science courses for which academic credit can be awarded. No longer must the nurse anesthetist program be chained to the hospital where the temptation is to utilize its students to provide service in return for education. The potential for obtaining federal funding for such programs is yet to be put to the full test; however, a program structured within the university will be in an extremely good position to obtain such funding when it is available.

I am, of course, vitally interested in sound education for nurse anesthetists. I am devoting my professional life to seeing its development progress. At the Medical College of Virginia, we are committed to elevating standards for nurse anesthetist education. With the cooperation of the University officials, we are seeking to develop a meaningful curriculum around which we will train and educate the nurse anesthetist of the future at the baccalaureate level. My colleagues in similar positions are no less dedicated. We foresee the day when all Schools for Nurse Anesthetists will have faculties trained at the university-based schools, with the credentials to provide sound educational experiences for their students. We foresee the day when all nurse anesthetists will be assured of equivalent education. We encourage the cooperation and guidance of the American College of Anesthesiologists to play a greater role in the development of these programs.

It has been said that an anesthesiology residency cannot be successfully conducted within a hospital where nurse anesthetists are also being trained. I believe we have shown that it can be done. If anything, dual programs can serve to reinforce and complement each other, and it is the most practical way to develop the attitude of team practice at an early stage. Nurse anesthetists and residents trained together quickly see the advantages of each other. This serves to develop a healthy attitude among the trainees working together.

Currently, our nurse anesthetist program requires a two-semester intensive basic science course during which clinical experience is limited to developing basic techniques. Following this, the students' education is oriented to the clinical situation where they spend a period of one year administering approximately 750 anesthetics. The clinical instruction also includes affiliation with community and military hospitals so experience may be gained with all types of anesthesia techniques in various environmental situations. We would like to think that this program will serve as a model for emerging university-based programs. At the same time, however, we stand ready to learn from others if such learning will improve our standards.

In summary, I call upon anesthesia educators to abandon technician-training programs and instead help us develop nurse anesthetist programs to a higher level nationally. Let us remove our finger from the panic button and begin working together as a team, acknowledging our shortcomings and limitations. The time for us to establish the strongest possible ties both in our educational systems and our service-oriented institutions is right now. Mutual respect and cooperation are the keys to a smooth, efficient operation of an anesthesiologist-anesthetist team. And finally, let us be certain that the next meeting with the format of "What Is New in Anesthesiology" does not require a lecture on the anesthesia team.

Anesthesia, 1972*

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Implied in a title such as this one is an obligation to determine the present "state of the art," or science, if you will, and to elucidate, in a manner of speaking, where we are, why we are, and in which direction we may be going. To perform such a function in perspective, we must return to the past. Then one wonders, how far into the past? How much of the past is really relevant to today?

Our reflection will go back thirty years to 1942, in Montreal, Canada, to the sphere of McGill University. In those days, Montreal was on a full wartime basis: there was rationing of food and gasoline; soldiers, sailors, and airmen were nudging each other on the streets; the news on the radio was grim except for the occasional sparkle and lift from Winston Churchill; and in the midst of this, four young men, of whom only one is alive today, had been directed by the Canadian Army to pursue a course in anesthesia. The instructors have now become legend. Wesley Bourne was a teacher supreme, whose every sentence and intonation added knowledge to those who would listen, whose every movement at the head of the table was a superb action on a stage. Digby Leigh was the man who breathed life into the pediatric patient when it would appear none was there; he is the man who forged the subspecialty of pediatric anesthesia to make it what it is today. And Harold R. Griffith who is best known to all of us, probably not because of his quiet, lovable, unassuming, Rock-of-Gibralter character, but because in that year, 1942, he demonstrated to the world that curare, or intocostrin, as the preparation was called, could produce reversible relaxation of muscles and so immeasurably aid the performance of anesthesia and surgery.

In passing, it is worth noting that "Uncle" Harold, as he is known, was primarily a clinician. If he had been a habitué of the laboratory, the introduction of curare into practice might have been delayed. Doctor Lewis Wright, the eminent anesthesiologist from New York, had told him that curare had a bad record in dogs, producing marked salivation and significant hypotension. But Dr. Griffith, with his clinical acumen, recognizing that humans are indeed different from dogs, assayed the drug in his patients, his surgeon brother being a cooperative partner, and found it not wanting in desirable attributes.

It is fair to say that 1942 was a major turning point in our philosophy concerning anesthesia care for patients. Today it is rare for a patient to undergo major surgery without the benefit of muscle relaxant drugs. But other factors helped to shape the destiny which makes anesthesia the independent specialty it is at present. Out of the misery and suffering of the Second World War was spawned the anesthesiologist as a specialist; the man or woman who could preserve vital functions both during and after the ordeal of surgery, the individual who could balance, by dint of pharmacologic knowledge, a mixture of drugs, none to a toxic level, which would provide the correct degree of hypnosis, analgesia, muscular relaxation, and obtundation of reflexes for the performance of surgery.

The ubiquitous cautery forced a change in the habits of the anesthetist also. The standard ethyl ether, which had served so well for so long, and the almost angelic properties of cyclopropane were pushed into the background, albeit with some measure of distaste in certain quarters. The value of intravenous narcotic analgesics, to supplement the analgesia of nitrous oxide, became established first in 1953, and then with a vengeance in recent times. But in the interim came the overwhelming tide of

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the halogenated compounds best exemplified by halothane, which to some anesthetists has been all things to all patients, except for a little thiopental and muscle relaxant thrown in from time to time.

This period of growth and development was paralleled by a sharpened interest in what effects anesthetic drugs had on the vital functions of respiration, circulation, and renal and hepatic metabolism. Sophisticated experimentation in laboratories became the order of the day, and much valuable insight has been gained. In the operating rooms, monitoring has become a concomitant of drug administration, and the variables associated with arterial blood determinations and central venous pressures, to say nothing of an infinite variety of ventilators, are lending an aura of science to our pursuits.

And so we come to February 25, 1972. Where do we find ourselves today? If one looks at this program, if one listens to any series of papers discussing anesthesia practice, one finds a querulous note, a feeling approaching dismay, an uncertainness of attitude, a tone of belief that almost encourages disbelief. It appears that we are standing on the brink of change. But what change and in what manner?

As one surveys the scene, it is discouraging to see that a significant mortality still is attached to the process of anesthesia. One out of every 2,000 to 2,500 patients who submits to anesthesia becomes a statistic due in part to what anesthetists do or do not do. However effective the anesthesia administered, it is still not safe to the degree to which air travel, for example, has become. As a matter of fact, the risk of anesthesia today is probably of the same order as it was in 1942. There is pride that more extensive surgical procedures can be accomplished and that the elderly can survive a sojourn in the operating room, but cardiac arrest carts seldom manage to accumulate dust, and the morbidity-mortality conferences are still an active feature of training programs.

Of course, an element of risk will probably exist until the secret of the state called anesthesia becomes unraveled to some extent. Whatever we do now is associated with physiologic trespass, and what is needed is specificity of action that will not be associated with deterrents such as cardiovascular or respiratory depression.

We are losing faith in cherished pharmacologic traditions. Until seven or eight years ago, the stability of the inhalation anesthetics, except for trichloroethylene, was accepted as an inviolate statute. Then it became recognized that biodegradation was a problem with which to reckon, and that such metabolism could be influenced by numerous factors. Some of these were perhaps genetic in origin, some were related to other drugs acting as enzyme inducers, and at times even an anesthetic was acting as its own inducer of metabolism. The full significance of the fact that so-called stable anesthetics can be metabolized has yet to be delineated, but in the meantime the caution flags are being displayed, and our former confidence in these drugs is being shaken.

Not so many years ago, America's leadership in pharmaceutical discoveries was second to none. In 1958, for example, some 60 diagnostic and therapeutic compounds were marketed; by 1969, however, this number had dwindled to five or six. The principal stumbling block in this decline and fall has been the federal Food and Drug Administration. Efforts to satisfy the requirements and demands of this agency relative to a New Drug Application have become so frustrating that few pharmaceutical companies believe realistically that the time and work involved are worth the problems which must be surmounted. Anesthesiology is one of the specialities suffering from this frustration. The situation at the moment is that a number of new drugs are in actual use in many parts of the world but are not available to physicians in the United States. For example, a new muscle-relaxant drug, pancuronium, has supplanted d-tubocurarine in a number of countries, and bupivacaine, a long-acting local anesthetic, has been heralded in Europe; but both drugs are banned from general use in this country at the moment. Inability to participate in clinical trials of therapeutic compounds has dampened the enthusiasm of many anesthesiologists.

Also of deep concern to practicing anesthesiologists is the almost lackluster interest in the specialty by both the public and neophyte physicians even though, and perhaps because, our malpractice premiums are the highest in the medical profession, ranking with those of our surgical colleagues. It is discouraging to see some of our leaders forsaking the field for administrative pursuits. Paradoxically, others are fleeing the operating room to become specialists in intensive care or inhalation therapy. The rationale for this escape is that the graduating medical student is more likely to be attracted to this specialty if the anesthesiologist accepts more re-

sponsibility outside the operating room, if he becomes recognized as the authority in acute medicine throughout the hospital. But what about the patient with the "cardiac arrest" back in the operating room?

Because of the foregoing, it is appropriate to say that in 1972 everything in anesthesiology is not wine and roses. Nor is it, of course, in the entire medical profession. The specter of National Health Insurance hangs heavy in the offing, the peer review system is rearing its head, and the recertification threat is ruffling the equilibrium of some. But how can we set our sights in anesthesia so as to rid ourselves of the indecisions, the frustrations, the lack of satisfaction with what we are doing, and move forward to provide safe pain relief for all patients in this country?

As noted, the arsenal of drugs upon which we have come to rely is being reduced in number and breadth of application. And one finds a trend in many centers toward the use of drugs which are administered parenterally. It is perhaps worthwhile to explore this shift to see if indeed safe and efficient anesthesia can be provided by this means.

For purposes of discussion, certain ground rules will be established which will serve to shape the nature of the search. First, let us suppose potent inhalation anesthetics will be discarded. Second, it will be assumed that the anesthetists can adequately assist or control ventilatory exchange. Third, a primary aim will be to maintain cardiovascular dynamics, with preservation of the preexisting blood pressure and, one hopes, perfusion of blood to the organs in the normal preferential manner. Fourth, the central nervous system will be sufficiently obtunded so the patient will have no memory of the anesthetic or surgical procedure, and painful stimuli will not be reflected in abnormal reflex reactions. Fifth, adequate conditions will be provided for the contemplated surgery, with sufficient signs being presented early to indicate the need for blood volume replacement. And last, there will be rapid restoration of central nervous system function at the conclusion of surgery, with the patient oriented to time, place, and person, and showing evidence of normal respiratory and cardiovascular functions. Ideally, analgesia will be extended into the postoperative period.

Actually, there is nothing really novel in these aims. In 1953, in Liverpool, England, Cecil Gray described in detail what has come to be known as the "Liverpool Technique," which incorporates a "sleep" dose of thiopental, approximately 250 mg for a 70 kg adult; a moderate dose of d-tubocurarine (35 to 40 mg) to facilitate endotracheal intubation and provide muscle relaxation; and a 70:30 high-flow mixture of nitrous oxide and oxygen, plus hyperventilation, to provide analgesia and central nervous system obtundation. The hyperventilation is important in this sequence as it contributes to the cerebral obfuscation. Anesthesiologists in America have questioned this technique on several counts. Thiopental is a direct cardiac depressant and is capable, even in small doses, of producing cardiovascular depression, particularly in geriatric patients. Relatively large doses of d-tubocurarine can also produce marked reductions of blood pressure in some patients, particularly when used in association with thiopental. Administration of only 30% oxygen, especially in patients with preexisting pulmonary dysfunction, has been shown to result in critically low arterial oxygen tensions during the course of anesthesia. Hyperventilation, if carried to the point of reducing arterial carbon dioxide tension to less than 25 mm Hg, may result in a degree of cerebral hypoxia. And finally, there are a number of reports in the literature which attest to the fact that with this technique patients can on occasion recall events which transpired during surgery.

Because of questions such as these, anesthesiologists are modifying their approach to the Liverpool Technique. The basic soundness of using nitrous oxide for its amnesic and analgesic properties is not being questioned, and indeed it forms the foundation upon which the anesthetic structure is mounted. (Incidentally, there is no evidence at the moment that nitrous oxide undergoes biodegradation in the body.) However, it is recognized that nitrous oxide is not all things to all patients and that the degree of amnesia and analgesia which it confers varies from one person to another. Moreover, its actions are dose-related, so that if it is believed necessary to provide a patient with 40 or 50% oxygen during surgery, the benefits from nitrous oxide will be reduced accordingly.

One of the more striking applications of an intravenous drug to modern surgery has been the use of the tried-and-true morphine in open heart procedures, certainly a type of surgery which taxes the skill of all concerned. The doses employed are not niggardly (1 to 3 mg per kg), and there is now reasonable evidence that, at least in the normal

heart, doses of this order have little effect in depressing cardiac output. However, problems can arise with this approach. Some patients in incipient cardiac failure develop hypotension with only small doses of the drug, and careful titration is necessary. Although the analgesic properties of morphine are obvious, its propensity to produce amnesia is not great, and one wonders at times about recall by the patient. Another difficulty which is seen frequently, particularly in patients having coronary artery bypass procedures, is a worrisome degree of hypertension. There is concern about such increases in blood pressure; something which we have not had to worry about since the days of cyclopropane. One wonders if there is to be an alteration of blood pressure under anesthesia whether it is safer to have an increase rather than a decrease of 30 to 40 mm Hg. The reason for the increase in blood pressure is unknown at present. The two most likely causes are an augmentation in cardiac output and/or peripheral vascular resistance. The underlying etiology could be an increase in catecholamine release, perhaps due to the direct action of the drug or to reflex responses, which would imply an inadequate degree of anesthesia. Whatever the reasons, various ways of reducing the blood pressure have been employed. The administration of a low concentration of halothane (0.5%) is corrective, perhaps because of its sympatholytic effect or because of the added anesthesia it provides. The ganglion-blocking action of trimetaphan (Arfonad®) will often result in a reduction of blood pressure, and the adrenergic-blocking effect produced by chlorpromazine, and to a lesser extent by droperidol, will tend to restore the pressure toward normal levels.

The use of morphine in large doses also poses a problem related to metabolism in that its respiratory depressant effects persist beyond its period of usefulness in the operating room. This prolonged effect may be advantageous in open heart surgery in which it is planned to maintain the patient on artificial ventilation for a period of time, but it does present difficulties in other types of major surgery when one would like to have the patient self-sufficient in the recovery room. Perhaps the properties of the specific narcotic antagonist, naloxone, can be used to advantage under such circumstances.

Another narcotic combination, Innovar®, has met with varying degrees of success in its application to the state of anesthesia. The advantage of its narcotic component, the potent analgesic fentanyl, lies in its relatively rapid rate of metabolism, a given dose being effective for not more than 30 or 40 minutes. Therefore, with attention being paid to its titration, respiratory depressant effects need not be a problem in the postoperative period. The other component of Innovar, the butyrophenone droperidol, has brought an exciting new dimension to what we are trying to accomplish in anesthesia. Probably acting at the level of the reticular activating system, this drug serves to disconnect the patient from the fear and concerns associated with his immediate environment. However, the degree of associated amnesia is variable from one patient to another, and one cannot count on a given dose of droperidol blotting out remembrance of a procedure. Although it has mild adrenergic-blocking properties, there is no evidence that it is a direct depressant to the myocardium and, if the patient remains supine and does not have a reduced circulating blood volume, vascular homeostasis is preserved with its administration. It also possesses anti-arrhythmic properties which help to stabilize cardiac rhythm during surgery. Unlike fentanyl, droperidol is metabolized slowly in the body, its effects lasting six to eight hours, so that its actions are apparent in the recovery room. These effects are deemed advantageous by some: it is not a respiratory depressant, nor is it an analgesic, but it does appear to alter the patient's reaction to pain so that he does not demand narcotic analgesics.

So far, the drugs discussed have not demonstrated evidence of potent amnesia, or ability to prevent recall—the best has probably been nitrous oxide. But a relative newcomer on the scene, diazepam, shows evidence of providing the desired potency. Administered intravenously, the dose of diazepam required to produce a lack of subjective response by the patient is highly variable, ranging from 5 to 30 mg or more, but amnesia for associated events is usually present after a dose of 10 mg. Best described as an amnestic and hypnotic, in that order, diazepam can produce respiratory depression but has little effect on cardiovascular hemodynamics in the doses required for hypnosis. It can be used safely and with merit in association with narcotics and muscle relaxants.

One compound which has had a mixed reception since its introduction in 1970 is ketamine. Enthusiasts have embraced it because it produces unconsciousness and intense analgesia without associated depression of respiration, except mo-

mentarily in some patients, or circulation. As a matter of fact, cardiovascular dynamics appear to be enhanced, as reflected in a moderate increase in pulse rate and blood pressure. Interestingly enough, this cardiac stimulation is not associated with an increase in myocardial irritability; in fact, the drug possesses anti-arrhythmic properties. Equally important is the safety of the compound: more than five times the recommended clinical dose can be given intravenously without untoward effects in a healthy patient. Detractors point to the relatively high incidence of hallucinatory phenomena in adults as they are recovering from the effects of the drug when it has been used as the principal anesthetic. They also emphasize the random movements and increase in muscle tone seen in many patients.

The mechanisms of the action of ketamine have not been well defined, nor is its sphere of usefulness in the field of anesthesia clear at the moment. Does the lack of respiratory and cardiovascular depression in the presence of apparent unconsciousness and intense analgesia imply that this classification of chemical compound allows one to narrow down the actions which one wishes to provide for the anesthetic state? Does the wide margin of safety in dosage imply an inborn compensation for errors of administration? One could validly criticize the upsurge in cardiovascular dynamics associated with administration, as one does with the narcotic drugs. But is such a change as deleterious as the cardiovascular depression so often noted with conventional anesthesia?

If the reasons for the increase in vascular dynamics were known, one might be able to compensate for it directly. Such an increase could result from direct stimulation of the vasomotor center; it could be secondary to an increase in catecholamine secretion; or as Dowdy has suggested, it could be due to an alteration in the baroreceptor mechanism. Whatever the cause, small doses of droperidol (2.5 to 5 mg I.V.) tend to return the blood pressure toward normal levels.

With the intravenous drugs which are at present being used to supplement the Liverpool Technique, it is apparent that full reliance must be placed on muscle relaxant compounds to provide satisfactory operating conditions for the surgeon. What Griffith began in 1942 will probably continue in full force, no doubt with substitutions for d-tubocurarine from time to time.

One would like to elaborate on one modification of the nitrous oxide, curare technique which is being presently evaluated. It pertains to the substitution of ketamine for thiopental. Following conventional narcotic or Innovar premedication, induction of anesthesia is with ketamine 2 mg per kg intravenously, followed by d-tubocurarine approximately 0.5 mg per kg, endoctracheal intubation in about three minutes with topical analgesia to the larynx and trachea with lidocaine 4.0% solution, and then maintenance with nitrous oxide and oxygen in a 60:40 mixture. Increments of ketamine 20 to 30 mg are given just before the skin incision and at intervals thereafter. Total dose of ketamine for a three-hour procedure is about 300 mg. Controlled respiration with moderate hyperventilation is maintained, and increments of d-tubocurarine 6 to 9 mg are administered as required to maintain muscle relaxation. Neostigmine reversal is carried out at the end of surgery, and the patient is usually oriented and answering questions before leaving the operating room. In 50 such experiences, there have been no instances of hypotension. In a few patients, increase of systolic pressures of the order of 30 to 40 mm Hg has been controlled by small doses of droperidol (2.5 to 5.0 mg I.V.). In no patient has there been unusual reaction following surgery, and in none has recall of the surgical procedure been elicited.

It is apparent that there are a number of ways in which one can approach fulfillment of the criteria posed. None is perfect, and probably none will be until the secret of anesthesia is unmasked. In the interim, each of us can and must work toward the goal of effective and safe anesthesia.

If indeed we turn our backs on the potent inhalation anesthetics, or use them perhaps only as a second line of defense, we will no longer have need for the cumbersome anesthetic apparatus in use at present. Our gas machines are imposing and perhaps awesome to the non-anesthetists in the operating room, maybe even lending an aura of mystery to our operations at the head of the table. But such displays of one-upmanship are really no longer necessary in our profession. So one would propose scrapping the conventional flowmeters and de-emphasizing the anesthetic machine as a central focus and substituting primarily a ventilating apparatus. Such a ventilator would be volume controlled, pressure variable, simple and foolproof in construction, and capable of being sterilized with ease. It would also be capable of providing positive to atmospheric, positive

to negative, or positive to positive pressures, with such pressures immediately identifiable on a rugged but accurate pressure gauge. The rate of respiration per minute would be under the control of the anesthetist, as would the tidal volume to be delivered, this tidal volume being constantly displayed on a ventilation meter. The length of the inspiratory and expiratory phases of ventilation would also be subject to variation by the anesthetist, although the standard to be employed would be the 1:2 ratio proven to be so satisfactory by Cournand a number of years ago. Of vital importance would be a means of manually ventilating the patient at a moment's notice, and of being able to alternate in a simple manner between mechanical and manual ventilation.

The gases to be supplied to the ventilator would be nitrous oxide and oxygen, utilizing one meter to determine the total flow rate per minute and a mixing valve by means of which one could vary the percentage of each gas being supplied to the patient. This mixing valve would be unable to provide less than 25% oxygen and would of course have a fail-safe mechanism incorporated into it. In the gas supply line distal to the mixing valve would be an oxygen analyzer which would constantly record the percentage of oxygen in the mixture being delivered to the patient.

It is unlikely that a carbon dioxide absorber would be necessary in this ventilator-oriented apparatus—particularly with our present knowledge regarding controlled ventilation in the anesthetized patient—if the flow rate of the mixture supplied to the patient were not less than six liters per minute. However, an important monitor in this apparatus would be a carbon dioxide analyzer which would intermittently, or on demand, record on a scale both the inspired and expired concentrations of carbon dioxide.

Such would be the basic components of a new anesthetic apparatus. It would be mechanically simple and incorporate a number of monitors vital to the welfare of the patient which are not an integral part of present-day equipment. Of course, for those who wished to rely in part on the potent inhalation anesthetics, calibrated vaporizers could be placed in series on the patient side of the mixing valve.

One would hope that more specific means of monitoring the integrity of the cardiovascular system in a non-invasive manner will become available in the operating room. Today we rely primarily on the blood pressure and the electrocardiogram. The blood pressure is the result of the interaction between the cardiac output, the peripheral vascular resistance, and the circulating blood volume, and therefore, changes which occur cannot be specifically diagnosed. The electrocardiogram merely reflects the electrical activity within the conduction system of the heart; it reveals little concerning myocardial function or cardiac output per se. The closest one can come to determining the adequacy of perfusion of blood to organs is to observe the urinary output. An adequate flow of urine during surgery reflects continuing renal function and presumably reasonable perfusion of that organ.

In proper care of the patient, increasing reliance is being placed on determinations of arterial pH and blood gas values, and rightly so. But obtaining comparative information over a period of hours or days requires an arterial puncture and usually an indwelling catheter, and because of this degree of invasive sophistication, many patients are being denied therapeutic measures which they might otherwise receive. A non-invasive technique of determining these values is sorely needed and capable of being perfected.

There is one other aspect of anesthetic practice in this country today which demands attention in the effort to enhance the safety and efficiency of our services. We have the unique situation of two groups of professionals, anesthesiologists, some 10,000 in number, and nurse anesthetists, some 14,000 in number, being responsible for anesthetic care. Unfortunately, until recently, for reasons which one hopes are now past history, there was little liaison or rapport between these two groups, even though their daily objective was the same—to provide the best anesthetic care possible for the patient. It is high time we began to communicate meaningfully with each other, recognizing the concept that by working together, by sharing mutual problems, better care will be provided for the patient.

Beginnings have been made in these directions. There is a Liaison Committee of the American Society of Anesthesiologists and the American Association of Nurse Anesthetists which meets regularly in a growing spirit of mutual exchange. Both societies have recognized a joint statement of over all aims and objectives. Meetings such as this one attest to the fact that not only are nurse anesthetists sharing as participants in scientific programs, but they are also attending in greater numbers such programs throughout the country.

But there is more to be done. We need to work together as individuals, as small groups within a hospital, as larger groups within a city or state, and on a national level. Each of these groups has become a national entity in the realm of medicine and will remain so. The proper administration of anesthesia could not survive in this country without the full activities of both groups, and patients who require surgery are dependent on the knowledge and practice of both the nurse anesthetist and the anesthesiologist. It is my sincere belief that by talking together, working together, acquiring knowledge together, the practice of anesthesia in this country will become safer and more efficient.

There is one concrete way in which these mutual efforts could be enhanced. To increase our knowledge and abilities in this day and age, reliance is placed primarily on reading books and journals, and on attending meetings, workshops, and seminars. The latter efforts usually involve leaving one's place of practice and traveling some distance. What one would propose is that the teacher travel to one's place of work, spend a few days in the operating rooms at the head of the table, showing and telling, to put it in the vernacular, and discussing actual or potential problems which could arise. There is a precedent for this type of endeavor in at least one state of the Union in the speciality of obstetrics. It would be worthy of a trial in anesthesiology. One recognizes, of course, the numerous logistical and economic problems surrounding such a suggestion, but a national society or a national foundation could lend its support less wisely in other endeavors.

And so we end the survey of *Anesthesia, 1972*. If it has failed to be glowing and full of sparkle, it is not for lack of confidence that this, the youngest of the true specialties, has inherent within it the greatest challenge for the future. Today we are standing on the threshold of significant discoveries and developments. Everyone in this room will have an opportunity to participate in the exciting advances that are all about us. But while we work and extend our knowledge, may we keep in the foreground the hope and prayer that Sir Robert Hutchison left for us: "From inability to let well alone; from too much zeal for the new and contempt for what is old; from putting knowledge before wisdom, science before art, and cleverness before common sense; from treating patients as cases, and from making the cure of the disease more grievous than the endurance of the same—good Lord, deliver us."

Recent Developments in Anesthesia Malpractice*

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The very fact that I have been asked to participate in a program of this significance is indicative of an ever increasing problem that is facing all facets of the medical profession—that is, how to stay in the hospital and out of the courtroom. I shall be talking about some of the general considerations all of you, as anesthesiologists, anesthetists, and physicians, should keep in mind in order to understand your legal responsibilities to the patient.

The topic "Recent Developments" is partially a misnomer because what I am going to address myself to is the recent trends or developments in three particular areas of the law as it affects the field of medicine, and then attempt to relate these particularly to the field of anesthesiology. You must also understand that "recent" medically and "recent" legally may in fact be years apart. What are commonly referred to as recent legal theories, frequently find their origin in court decisions several decades old. At the same time, some of what follows is of such recent vintage as to be classified by a vintner as green.

First, I would like to discuss the physician's duty to inform his patient and the recent legal developments in the area of informed consent. Second, I will discuss briefly the area of potential contract liability which is somewhat related to informed consent. And last, some of the more classical legal problems involving a physician and his patient, with special emphasis on the Captain of the Ship Doctrine and respondeat superior.

While the time has not yet arrived, and hopefully never will, when a physician cannot go about his daily tasks without having a copy of *Gray's Anatomy* in one hand plus *Corpus Juris* in the other, education as to the legal aspects of the practice of medicine in recent years has or should become a required course of study in our nation's medical schools and colleges. It is with this thought in mind that I present to you today's discussion.

Informed Consent. The Doctrine of Informed Consent is the child of the Doctrine of the Inviolability of the Individual Body, a concept born of the common law. Thus, it was stated in a recent case that "Anglo-American law starts with the premise of thorough-going self-determination; each man is considered to be master of his own body and he may, if of sound mind, expressly prohibit the performance of life-saving surgery, or other medical treatment, and while a doctor might well believe that an operation or a form of treatment is desirable or necessary, the law does not permit him to substitute his own judgment for that of the patient by any form of artifice or deception" (1).

It is because of this deep-rooted concept that, prior to any treatment, a physician must obtain his patient's consent. Valid consent to treatment can be obtained in any of several ways. First, the physician can obtain the *express* consent of the patient. This is done either orally or in writing, and most hospitals now have some type of consent form, though frequently inadequate. Second, consent may be *implied in fact. Implied in fact* consent occurs when a patient knowingly accepts treatment, as in rolling up his sleeve for an injection or agrees to an examination by lying on the examining table. Third, consent may be *implied in law.* Such consent occurs when the patient comes to a hospital unconscious or an emergency condition arises whereby he is unable to acknowledge his consent to treatment. Finally, consent may be given by a parent or guardian in the case of a child or incompetent.

For various reasons, the consent given may be a nullity. For instance, the consent may have been

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given by one who had no authority to give it, or it may have been obtained by fraud or misrepresentation on the part of the physician. While most physicians are aware of these traditional reasons for invalidating a consent, a relatively new reason for such has developed in recent years. Thus, courts have held with increasing frequency that a patient's consent must be informed and intelligent in order to be valid. The patient must have a clear understanding of what procedure is to be performed on him and the risks and possible complications involved. A disclosure that falls short of this test can invalidate the consent given just as thoroughly as if it had been obtained through fraud.

While actions at law have always been available to patients against their physicians for fraudulently induced consent or for operations performed without consent, only recently have actions at law been maintained by patients who allege that although their consent was given, it was invalid due to the physician's falling short of his duty to inform. This new right of action appears to have its genesis in the dictum† of a Virginia case, *Hunter v. Burroughs* (2), decided in 1918. In this case, the plaintiff was suffering from eczema and the defendant/physician recommended x-ray treatment as a cure. Back in 1914 such a treatment was revolutionary, and the defendant failed to warn the plaintiff of the risk of possible burn involved in its use. The patient suffered severe burns and sued his physician on two theories. First, he alleged that the treatment had been administered negligently; and second, he alleged that the physician failed to warn him of the possible dangers of x-ray treatment. The court affirmed a judgment for the plaintiff on his negligence theory and thus did not have to reach the issue of informed consent. However, in a dictum, the court laid the ground work for later court decisions on informed consent (3).

The basis of such an action is that a patient cannot give a valid consent to a treatment which he knows little or nothing about. The inviolability of the individual body necessitates that any consent given must be based on information necessary to make the consent intelligent and freely given. This includes the duty of the physician to disclose to his patient all relevant information concerning a proposed treatment, including the collateral risks and complications attendant to the treatment, so that the patient's consent would be an intelligent one based on complete information. The modern action based on a lack of informed consent did not fully develop until 1960 in the case of *Natanson v. Kline* (4), a case very similar factually to the *Hunter* case.

In the *Natanson* case, Mrs. Natanson had undergone surgery for the removal of a cancerous lesion in her left breast. As a precautionary measure, her physician, Dr. Kline, advised that she undergo radiation therapy to prevent further spread of the cancer. Mrs. Natanson consented to such treatment, but as a result of it, suffered severe burns. Subsequently, Mrs. Natanson brought an action against her physician on the theory that the consent to treatment was not informed. The Supreme Court of Kansas held that Dr. Kline was under the affirmative duty to make reasonable disclosure to Mrs. Natanson, allowing her to make an intelligent decision whether or not to take cobalt treatment. This duty included disclosing the risk inherent in the proposed course of treatment, but was limited to the disclosure only of facts necessary to form the basis of an intelligent consent.

In defining this basis, the court held that the degree of disclosure is to be measured by the standard of what a reasonable medical practitioner would disclose to his patient under the same or similar circumstances. Thus, the patient must introduce expert medical testimony in order to establish the community standard as to disclosure. Once such testimony is produced, it becomes a jury question as to whether the defendant/physician falls short of this standard.

Acknowledging the liability of a physician to his patient for failure to provide sufficient information necessary for an informed consent, the question arises as to what type of action is to be maintained by the patient. The courts themselves are somewhat confused in this regard but generally the action is brought on one of two theories: that of assault‡ or that of negligence. It is important to understand the difference between an action for assault and an action for negligence. In the former, the essence of the action being the unauthorized touching of the patient's body, the consent given, if there is any,

† Dictum—a statement of a principle of law in a decision by a court which was suggested by the case but was not necessary for a decision of the case as decided.

‡ The term technically should be "battery" which is an unauthorized touching of another's person; however, the courts have not been consistent in the use of this term, frequently using "assault" in place of it. The word "assault" is used generically to include both.

must be a complete nullity due to some misrepresentation or omission by the physician. On the other hand, negligence connotes the breach of some duty or standard of care imposed upon the physician. An example of an action for assault or unauthorized operation is the case of *Bang v. Charles T. Miller Hospital* (5), in which the patient was suffering from a urinary problem and, after consultation with the attending physician, consented to a transuretheral prostatic resection. The physician, however, failed to inform the patient that in doing the operation the spermatic cords would be cut and that the operation would render him sterile. The court held that the failure of the physician to disclose this essential fact rendered the plaintiff's consent invalid and hence, supported an action for assault. One of the key factors in an action based on assault is that lack of skill in performance of the operation or procedure is of no concern. The operation or treatment may have been performed in the most skillful manner but if there was no consent—informed consent—the plaintiff is entitled to recover damages from the physician. No expert testimony is needed in such a case.

A case closer to home is that of *Woodson v. Huey* (6), where prior to an operation the patient informed his physician that under no circumstances did he want a spinal anesthetic administered to him and was assured by the physician that he would receive a general anesthetic. The patient's wish was entered in his record by the physician. However, the anesthetist administered a spinal anesthetic following which the patient suffered paralysis. The court held the anesthetist liable for assault but not the surgeon. The fact that the spinal was given in a perfectly proper manner was of no consequence in an action for assault (7).

A negligence action, on the other hand, requires the plaintiff to show that (a) the risk was recognizable and the physician's duty of care required the disclosure of that risk; (b) had the patient known of the risk, he would not have consented; and (c) no justification existed for the physician's failure to disclose the risk (8). The plaintiff must prove the first element by expert testimony establishing the community standard and showing that the physician's actions fell short of that standard. The second element necessarily involves the subjective intent of the patient and can be established by his simply testifying that had he known of the risk, he would not have agreed. The third element comes into play only if the plaintiff can establish the first and even then would require expert testimony to establish the requirement of disclosure. (A few courts have placed the burden of proving this third element on the physician rather than on the patient, the effect of which is to create a jury issue in such cases.)

If these three elements are shown by the plaintiff, he has made out a prima facie case, and the defendant must counter by showing that he in fact did make adequate disclosure or that under the accepted standards, disclosure was not required.

Although a few courts still treat informed consent cases as an action for assault, the great majority of jurisdictions are getting away from this theory and are treating such as actions sounding in negligence; thus putting them in the same category as an action for mistreatment (9). Thus, in the case where the community standard is to secure consent to the administration of a spinal anesthetic during childbirth, it may be malpractice, that is, an action for negligence, where such consent is not procured prior to the actual giving of the spinal anesthetic (10).

Exactly what the courts require to make consent effectual is at the present time in a state of confusion. The Arizona Supreme Court has set down a good rule in defining consent:

> Consent . . . is effectual if the consentor understands substantially the nature of the surgical procedure attempted and the probable results of the operation. This, as a matter of law, constitutes an informed consent. . . . Given an informed consent, liability if any must be predicated in malpractice (11).

Coupled with the foregoing rule is the corollary being adopted by more and more courts that the primary duty of a physician is to do what is best for his patient, and that a physician may withhold disclosure of information regarding any risks or complications of the operation or treatment where a full disclosure would be detrimental to the patient's total care and best interest (12). Thus, when in the physician's professional opinion, informing the patient of certain of the risks or complications would make the patient unduly apprehensive and increase the risk of complications during surgery, information may be withheld. However, let me emphasize the importance of making a notation of such action on the patient's chart and, if appropriate, informing the patient as soon as possible after the surgery has been completed.

What then, as anesthesiologists, should you do, and tell your patients prior to the administration of anesthesia? Unfortunately, there is no hard and fast rule which can be stated as to the circumstances under which you can withhold making a full disclosure and as to the kind of information which can be withheld. Each case must of necessity depend on its own particular facts.

However, there are some basic guides that should be kept in mind:

1. Examine the patient prior to administering anesthesia, preferably the night before and this should be more than a cursory examination. Make a notation in the chart of the date and time of your examination, the findings, and any appropriate orders. Any doubt as to the patient's condition should be clarified because you will be held responsible for what could have been discovered by a proper physical examination. In the case of *Butler v. Layton* (13) negligence was found in the administration of ether to a patient suffering from a bad cold when the patient developed acute bronchitis which was caused by the anesthetic. However, where evidence is produced by the physician that a proper physical examination was given to the patient prior to administering the anesthetic, liability on this ground is usually avoided (14).
2. Explain generally the type of anesthetic to be administered, what will happen, and that there are risks and complications attendant to any medical procedure. Depending upon the patient's condition and emotional stability, make your decision as to how full a disclosure should be made. A fairly detailed explanation of what will take place may be of invaluable help since fear of the unknown is always much worse than fear of the known.
3. Have the consent form executed by the patient with any restrictions imposed by the patient noted thereon. If there are any restrictions these should also be noted in the chart. Incidentally, if there is any subsequent change as to any limitations on the previously given consent, this should be thoroughly and completely documented in the chart.

Contract Liability. As an adjunct to informed consent, let me give you a word of caution with respect to the assurances given to a patient. Courts have been severe in judging physicians who mislead, inadvertently or otherwise, their patients in regard to the potential seriousness or relative simplicity of a proposed procedure or operation. Thus, the physician who makes such statements as, "No danger can result" or "It's a perfectly safe treatment," may be held liable even though the operation he performs is done with all due care and competency. Illustrative of this is a recent case from Michigan (15), decided in 1971, in which the plaintiff was suffering from a peptic ulcer and contacted the defendant physicians regarding a possible operation. The patient was never told that he *must* have the operation, but the gist of what the defendant physicians told him is the following:

> Once you have an operation it takes care of all your troubles. You can eat as you want to, you can drink as you want to, you can go as you please. Dr. [X] and I are specialists, there is nothing to it at all—it's a very simple operation. You'll be out of work three to four weeks at the most. There is no danger at all in this operation. After the operation you can throw away your pill box. In twenty years if you figure out what you spent for Maalox pills and doctor calls, you could buy an awful lot. Weigh it against an operation.

The court held that such words amounted to an offer of a contract to achieve by the operation the condition described; that in reliance on the description, the plaintiff accepted the offer; and that when these results in fact were not achieved, the contract condition described was breached. A substantial jury verdict for the plaintiff based on breach of contract was affirmed.

The majority opinion held that the question of whether a contract exists is a question of fact for a jury in every instance. Obviously, if this decision were to be followed by other courts, the effect could be disastrous because it would severely limit physicians in their efforts to assure patients and calm their normal fears. There was a very strong and well-reasoned dissent, and I would hope and expect that the attitude of the majority of the courts would not extend this holding to the normal practice of encouraging the patient with reasonable assurances which although they may at times be somewhat exaggerated, are made with a therapeutic intent.

Captain-of-the-Ship or Respondeat Superior.

This now brings us to our next area of discussion. It involves a straight malpractice case with special emphasis on the Captain-of-the-Ship Doctrine or respondeat superior. The Captain-of-the-Ship Doctrine is based upon the long-accepted premise that the surgeon is in charge of all that takes place in the operating room and is, therefore, liable for it all. Respondeat superior simply means let the master respond for anything that his servants or employees may do.

By way of illustration, let me refer to a case that occurred in California which clearly illustrates the broad umbrella of responsibility that is frequently applied. The anesthesia was being administered by a first-year resident who was under the immediate supervision of an anesthesiologist who was responsible for supervising other operations at the same time. The anesthesiologist was a salaried member of a private group of anesthesiologists, which group through its chief was responsible for the anesthesiology training program. The residency program was under the joint sponsorship of the local hospital, the county hospital, and the state university. The chief of the anesthesiology group was out of the country at the time the incident occurred, but was ultimately responsible for the program and all that went on in connection with it. When suit was filed, the defendants included the resident, the supervising anesthesiologist, another anesthesiologist who came to their assistance, the chief of the group, the group itself, the local hospital, the county hospital, the state university, and the surgeons performing the operation. The case was ultimately settled prior to trial with all parties contributing with the exception of the surgeons. Anoxia and cardiac arrest developed during surgery apparently due to several factors, all of which were the responsibility of those administering the anesthesia. Recognizing the distinct areas of separate responsibility which is gaining wider acceptance by the courts, the surgeons did not contribute to the ultimate settlement of the case. The right to control is the basis for liability in situations of this type, and it can be traced from the resident all the way through the various people or organizations participating in the training program.

In spite of the broad implications of the Captain-of-the-Ship Doctrine, the courts pretty uniformly recognize the expertise of anesthesiologists and except in very unusual situations, do not impose liability upon surgeons for anesthesia malpractice nor upon anesthesiologists for surgical malpractice.

When the anesthesia is being administered by an anesthetist, we find less uniformity in the decisions and a greater willingness on the part of some courts to impose liability upon the surgeon for the negligent administration of the anesthetic. There are two cases in point. One, *Jackson v. Joyner* (16), is a North Carolina case in which a nurse who was an employee of the hospital negligently administered the anesthetic. The court held that while the operation was in progress, the surgeon had full power and control over all assisting nurses and that hence, the nurse administering the anesthetic stood in the position of a borrowed servant to the surgeon for the purpose and duration of the operation. In the case of *McKenney v. Tromly* (17) the court held that it was an admitted fact that the surgeon had the absolute right of control of all personnel in the operating room during the operation and hence, was liable for the negligence of any of these persons. These cases represent the extreme position and find their origin in the ready willingness of surgeons to testify that they are in absolute control of all that goes on in the operating room during the performance of the operation. This certainly is no longer true, and they are doing themselves a disservice by failing to recognize the distinct areas of responsibility that exist in present day medicine.

Certified Registered Nurse Anesthetists (CRNA) are highly trained specialists with more training and experience in the field of anesthesiology than the vast majority of the surgeons. Thus, even in situations where CRNAs have administered the anesthetic, courts are recognizing their expertise and the separateness of their function. They follow the principle that where several doctors or nurses have distinct and separate parts to take which require the undivided attention of each, only the one who failed to use due care in the performance of the part assigned to him should be held responsible. This is true unless it can be shown that one exercises or has the right to control the other (18).

In Virginia, the question of whether a hospital-employed nurse/anesthetist is an agent of the operating physician or the hospital is a question of fact to be determined by the jury and the main test, as in all agency situations, is who has the right to control (19).

As you can see, all of the illustrations that have been given were not necessarily anesthesia cases. However, the legal principles involved would apply equally to you as anesthesiologists, and they do illus-

trate some of the more troublesome areas from a medical legal point of view.

I hope you will all become keenly aware of the problem of informed consent, and when you return to your respective hospitals, check and see what type consent forms are now being used; see that they are updated, and do as some groups of anesthesiologists are doing and use your own consent form. Litigation in the area of informed consent has only been going on for approximately 20 years, and each year there has been an increase in the number of suits filed involving this problem. A good consent form and an appropriate discussion between anesthesiologist and patient would go a long way in reducing the amount of litigation on this point.

With respect to respondeat superior and vicarious liability, it is difficult to predict how the courts will treat this in the future. However, I am certain there will be more and more judicial recognition of the "area of expertise" principle, thus limiting liability to those actually performing a specific task. At the same time, you should not overlook the fact that one negligent act by a first-year resident can start a domino theory of liability, and this is particularly true in the teaching institutions. In such situations, there is no substitute for active and closer supervision by the teaching staff.

Finally, let me remind you that it is an integral part of your responsibility to keep your patients assured and their fears to a minimum. However, don't let your exuberance and self-confidence get the best of you to the point that you find yourself as the defendant in a breach of contract action as did the physicians in the Michigan case referred to.

Thank you for your kind attention and I trust that you can continue to avoid the legal pitfalls some of my colleagues are constantly putting in your paths.

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Oxygen Toxicity and Anesthesia: A Ten-Year Review and Overview*

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The awareness of anesthesia personnel in the entity of "oxygen toxicity" has been increased in the last ten years by the greater involvement in prolonged respiratory care, and concomitantly increased complexity of operative management. The realization that cyanotic heart disease and primary pulmonary insufficiency does not necessarily protect the individual against the occurrence of the pulmonary manifestations of the disease, and that further *realistic* delineation of the parameters of control is necessary, has focused an intense beam of critical reevaluation on present methods of anesthetic management and postoperative care. It is important to note that "oxygen toxicity" as commonly discussed, that is, the CNS, pulmonary, and eye manifestations, represents advanced stages of the body's adverse responses. More frequent and subtle changes are present, but often overlooked. This is particularly true in the less easily discernible effects upon electron transport systems, and interference with basic membrane and enzymatic function.

As individuals trained in the management of cardio-respiratory emergencies, anesthesia personnel may expect to be called upon professionally regarding problems related to the management of dysbarism and oxygen toxicity; particularly in view of the currently developing underwater industrial and agricultural interests producing greater numbers of exposed individuals and radically different environmental conditions complicating acute medical care. The feasibility of returning individuals to the surface is poor. This would necessitate prolonged periods of decompression and would introduce serious problems of logistics.

A good deal more emphasis should be placed on the continuing study of oxygen effects by anesthesia laboratories and the possible interaction of the gas with other drugs as related to liver and kidney function, enzyme activity, membrane function, and electron transport. The information obtained will have broad ramifications in our total understanding of uptake and distribution, rate, and excretion of the anesthetic agents currently utilized, and hopefully will lead the way to the introduction of less noxious and more easily controlled agents and a more careful and logical physiological approach to patient management.

Historical Review. The concept of "oxygen toxicity" is anything but new, dating back to the time of Lavoisier, and followed in 1849 by Smith's description of a fatal pulmonary "inflammation" after exposure to oxygen at 3-5 atm for approximately 24 hours.

Insofar as the impact on anesthesia is concerned, in the last 15 years, during which time the problems began to affect the care of patients, the primary consideration was the pulmonary manifestations of the "disease." Perhaps, "iatrogenically induced disease" would be a more appropriate expression. This concentration on the pulmonary manifestations was natural in a nonhyperbaric environment, particularly since anesthesiologists had been more intimately involved with sufficient oxygenation of the patient during surgery, and the maintenance of a proper airway.

Although equally concerned about acid-base balance, carbon dioxide retention, prevention of atelectasis, and a reasonably reactive and physiologically intact postoperative patient, it was not until four major alterations occurred in patterns of patient care that the dynamic characteristics of oxygen toxicity and its relationship to this particular specialty became more obvious. These changes were: (1) The advent of open heart surgery, using the pump-oxy-

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genator, with the special problems resulting therefrom, (hemolysis, air embolism, and marked acidosis). (2) The use of hyperbaric facilities for the surgical and medical treatment of patients with surgical, medical, infectious, and cardiovascular diseases, and their attendant acute threat of oxygen toxicity; that is, *central nervous system* oxygen toxicity (as well as pulmonary toxicity). (3) The progressive involvement in prolonged postoperative ventilatory care, using continuously assisted and/or controlled respiration by ventilators equipped with only limited controls governing inspired oxygen tensions; and the nonconcomitant realization that such care was inducing or producing toxic pulmonary and/or other manifestations, or at least it was increasing the risk of such problems. (4) The current interest in "halothane hepatitis," enzymatic activation and inactivation, and the basic metabolic consequences produced by anesthetic agents. Some of the biophysical-electro-chemical-enzymatic and substrate actions may indeed be similar, as will be discussed further. The fascinating, multifaceted, and increasingly *complex* interwoven nature of the *spectrum* of oxygen toxicity is now only barely appreciated. It seems obvious, and reasonable, that the answers lie in the most basic biochemical processes. The comments in this paper will be oriented primarily toward the clinical aspects of oxygen toxicity as it relates to the practice of anesthesia.

To continue historically, in 1927 the observation was made that cold-blooded animals were much less susceptible to the toxic effects of oxygen unless they were warmed to 37.5°C. At that temperature, even turtles developed fulminating pulmonary manifestations after exposure.

It is known that increased oxygen tension produces changes in the transmembrane potential of frog skin, as contrasted to frog sciatic nerve, and that these changes are irreversible (Gottlieb and Cymerman, 1970). These investigators postulate that the membrane changes are produced by advanced oxidation of the SH groups; that membrane lipids and lipid complexes may have been altered; and that ATP synthesis was inactivated. In a monumentally informative experiment carried out by Chapin and Hohl, one lung of a dog was inflated with 100% oxygen for seven days. The other lung was inflated with air. Only the lung inflated with oxygen showed the characteristic pulmonary changes of oxygen toxicity which shall be described in more detail below.

Dr. Phillip C. Pratt, a pathologist, now at Duke University and previously associated with the Ohio Tuberculosis Hospital in Columbus, was one of the first clinicians to fully appreciate the early onset and progressive course of pulmonary changes in patients exposed to relatively "innocuous" amounts of oxygen for a period of time. In 1958, he pointed out the similarity of morphological findings in a series of patients, some of whom had received oxygen, for as little as two and one-half days, administered via nasal catheter—not ventilators. He demonstrated capillary congestion and proliferation, followed by the appearance of diffuse fibrosis after a period of about two weeks. Other changes previously noted in experimentally induced pulmonary manifestations were hyperemia, hemorrhage, edema, atelectasis, and "inflammation." These changes had to be differentiated from atelectasis, intrapulmonary hemorrhage, infection, and postmortem alterations due to absorption of gas. A brief experiment followed wherein mice were exposed to 100% oxygen for 48 hours at approximately 740 mm Hg, controlling humidity and temperature. Some of these mice were sacrificed, then autopsied immediately while still in oxygen; others were autopsied after 3 hours in oxygen. There was a significant difference in the appearance of the lungs at postmortem. Air control groups were also used. The lungs of the mice exposed to oxygen, killed in oxygen, and delayed 3 hours before postmortem were hemorrhagic and liver-like in consistency and did not float, thus simulating the characteristic, classical changes of advanced oxygen toxicity, usually thought to occur after more prolonged exposures. Pratt presented the above information at the hyperbaric conference in New York in 1964, and it is particularly noteworthy that he made the following very pertinent comment: "Since this occurs in hospitalized patients receiving oxygen by standard methods such as oxygen tents and nasal catheters, it is apparent that the pulmonary response can result from exposure to atmospheres containing well below 100% oxygen and probably in the range of only 50% oxygen." Pratt went on to discuss the relevant points in making the morphological differentiation between capillary proliferation and the opening of previously "unrecognized" capillaries. (Author's note: "Unused" capillaries. High-oxygen tensions seem to *decrease* the size and number of capillaries utilized, at least in myocardial perfusion and in the brain, as will be discussed later). Pratt felt that vasodilation leading to capillary proliferation was the probable chain of events; that continuous exposure for 24 hours at a

time was necessary; and that intermittent exposures were not cumulative in nature.

In 1964, Heppleston and Simnett found that tissue cultures of pulmonary alveolar epithelium were especially sensitive to oxygen under one atmosphere and equated this exposure to air at 5 atmospheres. They surmised oxygen acts through enzyme inhibition and preferentially affects enzymes possessing SH groups (NS: the statement made previously regarding the transmembrane potentials in frog skins).

Pontoppidan and others have demonstrated similar changes, including the postmortem appearance of hyaline membranes, in patients following ventilation with high-oxygen concentrations. A great deal of emphasis in the last three or four years has been placed on this possible causal factor of patient morbidity and mortality. In 1970, this hypothesis was accentuated by Hamilton and Singer in a study of postoperative cardiac surgery patients. It was their conclusion that fear of "toxicity" should not preclude the administration of oxygen in those patients who needed it. A general opinion still seems to prevail at this time that cyanotic heart disease, and other conditions leading to ventilation-perfusion inequalities, shunting, venous admixtures, and subsequent low-oxygen tensions (and/or hemoglobin saturation), have a protective effect for the patient, and that high-inspired oxygen tensions can be used with considerably less concern. This conclusion is not necessarily valid, as shown by a case report from the Massachusetts General Hospital (New England Journal, May 1970), where it was disclosed that a patient died from pulmonary insufficiency with demonstrated fibrosis following prolonged artificial ventilation. Furthermore, a very important study by Hills indicates that the creation of an artificial shunt producing cyanosis does not necessarily protect an animal from pulmonary injury secondary to high-oxygen tension.

It appears that certain conditions can deprive the individual of protective mechanisms. Artificially altered physiology can produce changes in the reaction of molecular oxygen with SH groups and other enzyme substrates. This effect in turn upsets electron transfer balance and results in additional effects in certain types of cells and subsequently in certain organ systems or "target areas." These effects occur following the administration of such compounds as dipyridylium dichloride (Clements, Fisher, and Kenneth, 1970); or result from the interaction of other compounds producing changes in certain trace metals and inorganic phosphorous. Mn^{++} and Zn^{++} may have some effect in preventing the occurence of lung edema. Mg^{++} seems to have a protective effect against seizures resulting from high-oxygen pressures OHP (Radomski and Wood, 1970). Manganese may act by inhibition of mitochondrial swelling and lipid peroxide formation in the mitochondria; that is, an antioxidant effect. However, similar reactions may also occur producing an opposite effect; that is, sensitization of cells (see below).

The cumulative end results as far as the lung is concerned are: the changes in epithelial cell population; the accumulation of both interstitial and alveolar fluid; and/or proteinaceous material; the deposition of hyaline membrane material; and changes in "surfactant" and its properties. Diffusion is altered, an "alveolar-capillary block" situation develops, shunting occurs, and the patient then has a need for higher-inspired oxygen tensions to achieve any satisfactory saturation, while the "cure" is worsening the disease process!

The warning seems fairly obvious: A minimum oxygen concentration (inspired oxygen tension) should be used to produce an arterial tension of approximately 100 mm Hg and/or a normal hemoglobin saturation depending upon the individual.

Individual variations are very important and should be taken into consideration. These factors include: age, sex, temperature, acid-base balance, type and amount of hemoglobin, MHCH, diet, vitamin levels, and the administration of other drugs. Aspirin and ascorbic acid seem to augment toxicity (Serrill, *et al.*, 1971). Tocopherol deficient animals appear less sensitive to lipid peroxidation in the lung until ascorbic acid and ferrous ions are added (Raskin, *et al.*, 1971). Other factors such as smoking and resultant carbon monoxide levels (Rodkey, *et al.*, 1971) affect the response of the lung. Simple immersion to the head greatly intensifies the pulmonary reaction, primarily by promoting the formation of atelectasis (Balldin, *et al.*, 1971). Stress and its effects, especially increased adrenal output, all adversely affect the individual, as does increased thyroxin.

Conversely, thyroid blockers seem to have a protective effect, as does the administration of sulfhydryl group donors. Others compounds such as ANTU (alpha naphthylthiourea) may act by both actions; that is, by affecting thyroid hormone release, and by providing cellular sulfhydryl enzymes and cofactors in active reduced states (Mountain, 1963). If one can logically accept the argument that there

are individuals who are hypersusceptible to certain noxic or toxic stimuli or compounds, such as those individuals whose susceptible target areas are the red blood cells, which subsequently undergo hemolysis by the interaction with other drugs, then it is just as likely that certain individuals are "pneumonically sensitive." These individuals may react adversely to similar circumstances with the lung as the "target organ."

Opposite circumstances may apply. Certain individuals are hyposensitive. They may react with *increased* resistance, or *decreased* susceptibility, to the action of what are usually considered to be "toxic" concentrations of oxygen. This concept would certainly account for variations from the "usual response," such as the one reported by Kydd: Mice exposed to 550 mm Hg oxygen for 30 days showed only a few of the classical pulmonary changes, but did develop changes in the blood vessels.

Some individuals are susceptible to the occurrence of atelectasis presumably due to absorption of gas (oxygen), plus other factors yet to be determined (Burger, 1967).

A good deal of work has been devoted to the effect of oxygen on succinic dehydrogenase activity in the lung. Until recently it was thought that this was the most important enzyme system affected. However, Bardell and Fowler concluded that other dehydrogenases in lung tissue seem to be more adversely affected. At any rate, return of activity is slow compared to exposure times; that is, 6 hours of exposure to oxygen produced inhibition of the enzymes which returned to normal only after 12 to 48 hours. Interestingly enough in one study pentobarbital seemed to have a protective effect. This conclusion is in contradistinction to the usual *nonprotective* effects of anesthetics against damage to the CNS (see below): Residual effects may occur even though convulsions are masked.

Viral and bacterial diseases may grossly alter the individual's sensitivity to toxic agents such as oxygen, and may produce changes in "target areas." (Mountain, 1963). Smoking has a marked additive effect for atelectasis to occur following oxygen exposure. One study indicates that smokers had an in-flight vital capacity loss three times that of nonsmokers (Browning, 1970). Adrenalectomy, chlorpromazine, and sympathetic-blocking agents may have a protective effect, as does hypothermia (Burrows and Edwards, 1970).

There seems to be a cross-tolerance between some compounds which are considered to be toxic themselves, such as Ozone and NO_2 (Mountain, 1963). Ozone is quite toxic and produces striking epithelial changes including hyperchromatism, hyperplasia, and inflammatory changes. Central nervous system effects also result. Some changes may occur after only a few hours of exposure (Suskind, *et al.*, 1970).

A number of interesting concepts have developed in regard to the pulmonary changes and the manifestations related to oxygen toxicity. A great deal of weight has been given to changes in "surfactant." Earlier, in 1962, the emphasis was on surfactant changes, modification, depletion, and interference with its formation. However, with increasing knowledge in the field, and increasing reliability of investigative techniques, it is beginning to appear that surfactant (changes) may very well be another "target," or, if not a "target," a "system," directly and indirectly involved; resulting from more basic biochemical alterations such as those mentioned above.

"Nitrogen osmosis" is a term referring to an effect produced by the "inert gas" nitrogen, wherein it can pull water away from other solutions of inert gases through certain types of membranes. This is now a popular concept in hyperbaric gas physiology. Such biophysical alteration may very well have some bearing on the mechanism of oxygen toxicity, and the narcotic action of certain "inert anesthetic gases" (neon, argon, etc.). During increased-inspired oxygen tension (thus increased arterial oxygen tensions [pO_2]) a gradient develops between the arterial tension of pO_2 and tissues. This has been called a "steady-state gradient." If certain physical circumstances are prevailing, the movement of water molecules may occur (Hills, 1971). Niinikoski and coworkers are under the impression that the primary effect of oxygen is on the capillary endothelium, producing an increased capillary permeability and a *secondary* "washout" causing a depletion of surfactant and other phospholipids not heretofore considered to be part of normal "surfactants." The mere presence or increase of lipids in such a "washout" does not therefore connote adequate surfactant activity. It may indicate only a "washout," and a depletion of alveolar surface tension reducing materials. Furthermore, one need not find peroxides of lipids, yet detrimental effects of high oxygen may have altered the structural lipids of cells by peroxidation and oxidation and produced subsequent changes in

cellular membranes. These in turn may lead to the release of proteolytic enzymes and even connective tissue elements may be released into the alveoli.

So finally having reached a discussion of "surfactant" after all of the above, it is with the realization that every aspect of "oxygen toxicity" is tied up with the mechanisms and biochemical utilization of the *transport* of oxygen.

Let us quickly consider the various aspects of alveolar-capillary diffusion pertinent to this discussion (Rankin, 1969). Diffusion can be defined as the movement of molecules of gas from an area of high concentration to an area of lower concentration. As mentioned above, there is direct bearing in relationship to arterial gas tensions. The movements of gases across the alveolar-capillary membrane is determined by: (1) the mean difference in partial pressures of gas on either side of the membrane; (2) the surface area of the membrane; and (3) the permeability of the gas through the membrane. The third is inversely related to the thickness of the membrane. It should be noted at the outset that the total distance for perfusion through the normal alveolar-capillary membrane and the surface lining layer, etc., is of very small magnitude in the *normal* lung; that is, in the order much less than one micron. The pulmonary diffusing capacity of any gas is determined by the ratio of the quantity of gas transferred per unit time over the mean differences in partial pressure, and is directly proportional to the solubility of the gas and inversely proportional to the square root of the molecular weight (density) of the gas. It is not easy to calculate either the alveolar oxygen tension or the pulmonary capillary tensions. Oxygen tension differences between the alveolar gas and arterial, end-capillary blood are due to incomplete equilibration between the gas and arterial, end-capillaries, and due to the effect of venous admixtures from areas of poor ventilation to perfusion ratios. It should be remembered that pulmonary diffusing capacity must be reduced by ⅔ before normal arterial oxygen saturation will be affected. This fact should be kept in mind in considering the so called "latent periods" involved in oxygen toxicity in regard to the lung as well as other organs. Diffusing capacity varies with whole body size, metabolic rate, age, levels of lung inflation, alveolar ventilation, intrathoracic pressure, body position, and distribution of inspired gas. The Hamman-Rich syndrome is a classical example of the unfortunate patient who requires increasing amounts of oxygen to his own detriment. There appears to be excellent correlation between problems in diffusing capacity and pulmonary membrane damage, (etc.). Do the increases in areas of poor $\dot{V}/\dot{Q}$ which account for much of the loss or decrease in diffusing capacity result from changes in surfactant alone with increased surface tension, or does there occur an increase in pulmonary vascular resistance secondary to the capillary proliferation and "granulation tissue" formation noted by Pratt as one of the toxic effects of oxygen (not the classical effects of hypoxia)? Capillary congestion, an earlier manifestation, may mask problems of diffusion since it will tend to balance them out.

What then is "surfactant," and how does it apply to the concept of oxygen toxicity as we know it in the lung? Many workers have been involved in the field for a number of years: these include Pattle, Clements and Fisher, Morgan, Sutnick, Said, Scarpelli, Tooley, and others mentioned above. A brief summary of their observations and conclusions as it applies to the topic under discussion is now in order.

Surfactant. It would be more appropriate to use the terminology "surfactant systems," "surfactants," or "alveolar lining materials." Unfortunately, until recently at least, the approach has been mostly an anatomical one, utilizing electron microscopy. The electron microscope has enabled investigators to find various structures not heretofore known and has led to certain hypotheses about the origin, function, and elimination of these lining materials. At the outset, it is very important to realize that the lung is not a passive organ responding to filling and emptying, but is a very active one in the body. With a surface area of approximately 70 meters square, and an estimated 300,000,000 alveoli, this fact is quite significant (Scarpelli, 1970).

In 1929, Von Neergaard noticed the differences between fluid-filled and air-filled lungs in the forces needed to ventilate, and pressure-volume relationships. Pattle, in 1955, noted the characteristics of pulmonary edema foam were such as to indicate lowered surface tension. This was followed by the work of Clements and others which showed that a surface-tension-lowering substance was present in lung tissue. Since then, biochemical analysis has indicated that the material is made up of a complex mixture of lipids, protein, and carbohydrates, chief among which is dipalmitoyl phosphatidyl choline (DPL) (palmitic acid). DPL makes up about 50% of the lipid fraction of the layer. This named lipid has been used interchangeably with "lecithin." It is

important to note that the surface-tension-lowering properties depend upon the presence of two *saturated* fatty acid residues. Included in the complex are albumin and carbohydrates (polysaccharides). In the lung, or alveoli as the case may be, a surface interface exists between air and a liquid or hypophase, lining the alveoli. The surface tension along the alveolar lining results primarily from molecular cohesive forces which produce a tendency toward collapse. This force is related to LaPlace's theorem which in turn relates surface tension (T) inversely to the radii of spheres and proportionately to the pressure of gas within the spheres or, as in this case, the alveoli, ($P = 2T/R$). The result is a tendency for liquid to form increasingly smaller spheres, leading to an ever-increasing tendency for collapse. This force is counteracted by the effects of the "surfactant groups," so that a new *end-surface-tension,* in actuality a surface pressure, results. This *surface pressure* force opposes the forces of plasma and other tissue fluids which have a surface tension of about 50 dynes per cm. Considerable elastic recoil results for the lungs. Fortunately, the tendency of the larger alveoli to become larger and larger as the smaller alveoli empty into them (following the above physical laws) is offset. Theoretically, at least, there is some uniformity to alveolar configuration and size, although there is now some doubt as to whether or not alveoli actually exist as true spheres. Maximum intra-alveolar pressures probably exist at the precise moment when the developing hemisphere at the end of the respiratory bronchiole has a diameter equal to that of the terminal respiratory bronchiole. Following this point, some instability and decrease in pressure occurs, with limits of expansion set by the elastic tissue of the lung, and so forth.

Surfactants are considered to be bipolar in nature and to assume this configuration anatomically in the hypophase boundary area. The choline, or *hydrophilic,* group is assumed to associate with the protein area of the hypophase: and the two hydrophobic fatty acid side chains become oriented toward the alveolar air side, forming a compressible film or surface-tension-lowering film. Increased compression, such as would result from collapse of alveoli, actually produces a decrease in surface tension. The result is an equilibration of tensions between the larger and smaller alveoli. The choline group, stated to be associated with protein, contains an ionized quarternary ammonium group which is stabilized by the presence of both calcium and sodium ions.

To summarize briefly: The activity and structure of surfactants is affected by a number of factors, including: (1) heat, which will reversibly inactivate it; (2) changes in pH; (3) the presence of blood; (4) electrolyte concentrations.

It is generally thought that surfactants are produced by "type II" alveolar cells and are secreted into the alveoli where they become incorporated into the lining layer. These are presumed by some to be found as cytoplasmic inclusion bodies, or osmiophilic lamellar inclusions. The inclusions are found in much lower numbers in those species (non-mammalian) lacking or having decreased surfactant levels. Two main theories exist: (1) that the giant alveolar cells form and secrete these organelles or inclusion bodies; or (2) that the opposite is true, the giant cells are responsible for the phagocytosis and breakdown of the surfactants, production being elsewhere—the nonciliated bronchiolar cell for example.

Nonetheless, synthesis turnover is rapid, C14 labeled phospholipids appear in pulmonary phospholipids within 5 minutes after intravenous injection, and a half-life of 14 hours is estimated for the surface active lecithins. It is possible that the entire lipid synthesis of lecithin occurs within the lung itself. The mechanisms of lecithin synthesis can take several paths, as has been nicely described by Morgan. Of import, in regard to the possible effect of oxygen on the system, is the rapidity of metabolism, equating the lung to the liver in some respects. This could produce a result so that any occurrence, physical or chemical, interfering with metabolic generation of either the lipids and/or carbohydrate and protein moieties might throw a natural "monkey wrench" into the system, thus accounting for the so-called *"latent period"* said to exist in the development of oxygen toxicity. The term "latent period" has very little compatibility with basic toxicological hypotheses. The presence of packets of surfactant might slow down the depletion rates and subsequent alterations in activity until such lack of activity produced a fairly rapid onset of symptoms and signs. There is no doubt that the situation is complex. Even the simple concept of a single layer of surfactant is under scrutiny and revision at this time.

Thus indirectly, oxygen may affect organ systems such as the lung through direct action at a very basic metabolic level. Surfactant changes are related to other clinical conditions such as the Respiratory Distress Syndrome of the newborn, changes following pulmonary arterial occlusion with

decrease in surfactant activity; and an excess of surfactant has been postulated in the disease of pulmonary alveolar proteinosis. One must bear in mind that multi-causal factors operate in these diseases, and that the inappropriate administration of "higher than needed" concentrations of oxygen (a somewhat ambiguous phrase) may contribute to the problems developing in various organs through the mechanisms discussed above.

Toxic Effects on Other Systems. Although the primary toxic effects of oxygen at less than one atmosphere (760 mm Hg) seem to be primarily manifested by changes in the lungs, or at least appear to be so orientated from the standpoint of anesthesiology, it is rather illogical to assume that all systems and organs in the body are *not* involved. The appearance of signs and symptoms is related to a time-dose factor, that is, related to exposure and/or circulation.

Two fundamental factors pertain regarding oxygen toxicity: (1) The metabolic consequences occur at the most basic levels of cellular and mitochondrial or membrane activity, and, consequently, must involve all areas of physiology and biochemistry within the body. (2) The "latency" of reaction should more appropriately be called the "time" of reaction. These considerations are certainly more in keeping with the basic toxicological principles of time-dose response. The intensity, duration, susceptibility of the subject, type of exposure, temperature, thyroid activity, presence or absence of other drugs, elements, and trace metals, the condition of the acid-base status, carbon dioxide elimination, 2-3 DPG levels, hemoglobin levels and types, sex, interaction and state of the adrenal-pituitary system and the sympathetic nervous system, perfusion, and other factors all determine which organ system will be affected and at what time.

Central Nervous System Toxicity. The toxic effect of oxygen at higher than ambient (760mm) pressures on the CNS ordinarily does not concern anesthesiologists unless they are operating under specific conditions of OHP in special chambers. However, the entrance of industry, agriculture, and other interests into underwater living and working conditions will produce a much larger population of individuals exposed to dysbarism and oxygen toxicity. It is logical to assume that medical personnel specially trained in cardio-pulmonary resuscitation, and so forth, will be called upon to assist in the diagnosis and therapy of such individuals. Furthermore, considering the basic nature of the processes of oxygen toxicity, one must have some reservations about the possible adverse effects of oxygen on the CNS at 760 mm or less, other than the well-known vasoconstrictive effects upon cerebral vasculature, and the tendency for hyperventilation which is commonly seen.

Classically, the CNS expression appears as a convulsion, usually beginning with more focal signs such as twitching about the mouth and eyes, and perhaps the small muscles of the hand. It is important to remember that mentation may be quite clear until the abrupt onset of the convulsion, which proceeds through usual tonic-clonic stages. Attempts at *decompression* during periods of glottic spasm may result in rupture of the lungs. Unlike the usual seizure, blood arterial oxygen tends to remain at normal or higher than usual levels if the patient is under OHP (oxygen-high pressure). Central nervous system toxic reactions are intimately involved with pCO_2 levels and acid-base balance, including lactate/pyruvate levels and ratios. Factors other than metabolic ones also pertain, such as circadian rhythms, which may alter the susceptibility to convulsions (Hof, *et al.*, 1971). At three atmospheres (OHP), animals treated with acetylsalicylic acid and/or ascorbic acid, and tocopherol deficient animals, began seizures earlier and died sooner than others (Serrill, *et al.*, 1971). The protective effect of magnesium has already been mentioned.

Anesthetic agents may mask the convulsions of oxygen toxicity, but do not appear to prevent the CNS damage produced by it which commonly results in spastic paralysis, and so forth. In fact, a recent and disturbing study by Lassiter has indicated that in the presence of only 5 psi, exposure to oxygen for two weeks (233 mm Hg) greatly reduced levels of acetylated and unacetylated coenzyme A in the brains of the animals. This occurred in the *absence* of overt signs of CNS toxicity. Apparently, nitrogen seems to have a "masking" or "quenching" effect, casting further doubt about its presumed "inertness." Coenzyme inactivation is postulated to result from: (a) direct oxidation of the sulhydryl groups; (b) from a block in synthesis, produced by oxygen itself through formation of oxygen-metal ion complexes; and (c) by the formation of free radicals elsewhere. These changes produce interference with the transfer of two-carbon units, with a subsequent block of glycolysis, and malfunctioning of the tricarboxylic acid cycle.

A recent paper by Kuperman has shown that the administration of oxygen following bilateral cordotomy may produce sleep-induced apnea, or "Ondine's curse," possibly through effects on the aortic-carotid reflex mechanisms. It can be seen from the above that the effect of oxygen on the CNS is quite complex and only now becoming more fully appreciated.

Effect of Oxygen on Red Blood Cells. As previously mentioned, one of the keys to understanding oxygen toxicity is a clear comprehension of the very complex and, up to now, not entirely clear mechanisms of oxygen transport and its relationship to membrane function.

If one acknowledges the fact that hypoxia per se is a marked stimulant to erythropoeisis, one would assume depression of bone marrow function upon exposure to high concentrations of oxygen. This is not necessarily the case, and the effect of high-oxygen tensions on DPG levels is not entirely clear. There are combined effects of increased pCO_2 levels, difficulties in "unsaturating" oxyhemoglobin, and resultant decreased pH levels (Astrup, 1970). Further influences of the pituitary and thyroid must be considered (Rodriquez and Shahidi, 1971).

Ascorbic acid and ASA may sensitize the red blood cells to lysis (Serrill, et al., 1971). Vitamin E deficient animals are markedly sensitive to the rapid destruction of rbcs, which in part is caused by the actual peroxidation of lipids in the rbc membrane. There appears to be a selective effect on older rbcs (Sabine and Leon, 1971). In certain susceptible animals, such lytic activity may occur at less than one atmosphere, manifesting itself by immediate effects on old cells, and delayed effects on the younger cells which demonstrate decreased mean potential life spans. A diet of alpha tocopherol, an antagonist to lipid peroxidation will abolish or prevent this lytic activity. Several areas are involved, including anerobic glycolysis, hexokinase activity, glucose 6-phosphate dehydrogenase activity, acetylcholinesterase activity, and specific gravity. It appears to be a membrane phenomenon. To confuse the issue even more, one study of angina pectoris and oxygen transport has indicated that its occurrence may actually decrease oxygen affinity of the hemoglobin without changes in DPG levels, possibly secondary to "humoral factors" (Shappell, *et al.,* 1970). One thing is certain, the various metabolic activities involved in oxygen transport and membrane function are not always predictable nor finite, and changes which occur under one set of circumstances may vary considerably under a slightly different set of parameters, adding to the complexity of response and interaction.

Toxic Effects of Oxygen on Liver and Kidney. With the current interest in "halothane hepatitis," and the renal effects of Penthrane®, more emphasis should be given to the possible toxic effects of other drugs and agents, and their possible interaction. The multiplicity of factors operating have been discussed above. In 1965, Felig reviewed the literature available on oxygen toxicity at that time and, supported by experiments in Wright Patterson Aeromedical Research Laboratories, came to the conclusion that evidence indicated the following: Exposures to only 258 mm Hg of oxygen for one week produced subcellular hepatic and renal alterations, visible on electron microscopy, in the *absence* of pulmonary histopathology. These changes included mitochondrial enlargement, clumping, and degeneration of membranes. Sodium lactate seemed to have a protective effect; lactate metabolism occurs through oxidation and the transfer of electrons to DPN.

Oxygen at tensions higher than one atmosphere increases lipid biosynthesis (Adams and Norton, 1971). On the other hand, oxygen may indirectly affect protein synthesis by altering dietary habits (Leon, *et al.,* 1971). This could be considered a subtle form of oxygen toxicity.

Insofar as the kidney is concerned, important findings relevant to kidney structure and function were reported by Hess and Menzel in 1971. In animals subjected to dietary depletion, particularly Vitamin A, a 35-day exposure to 100% oxygen produced changes in the proximal convoluted tubules, leading to an increase in lipid levels. These changes were presumed secondary to decreased fatty acid metabolism.

Conclusion. The adverse effect of overexposure to oxygen, that is, "oxygen toxicity," involves virtually every organ system in the body, including the lung, eye, kidney, liver, and erythropoetic systems. The effect follows classic toxicological principles, for the most part relating to time and dose of exposure, which in turn altered by the relative proximity of any particular organ to high-oxygen tensions. Obviously, the lung has the greatest exposure directly. The effect on other organ systems is primarily determined by the circulation and oxygen carrying and transport systems (Skinner, 1972; Siekevitz, 1970).

Most of the emphasis in this paper has been

upon the basic effects of high-oxygen tensions on enzymatic membrane and substrate systems, since it appears that altered biochemistry at these levels determines the ultimate manifestations of the toxic response, be it pulmonary, hepatic, ophthalmologic, and so forth.

More definitive criteria for controlling inspired and transported oxygen are needed. Even the presence of cyanotic heart disease with shunting and desaturation, or primary pulmonary failure per se, do not necessarily protect the individual against the deleterious effects of over-oxygenation. Thus a paradoxical situation develops wherein the administration of oxygen as a lifesaving measure eventually may produce fatal consequences.

Anesthesia personnel will become increasingly involved in situations related to such exposures to oxygen at high pressure (OHP) such as will be found in the new fields of industry and agriculture now being developed underwater, sometimes at great depths. It is the responsibility of the specialty to continue basic and clinical research in these areas and to expand clinical teaching to encompass the management of related problems.

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Proper Use of Mechanical Ventilators*

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The widespread use of mechanical ventilators over the past ten to fifteen years has greatly complicated respiratory care. As ventilators become more sophisticated, the requirement for physician knowledge becomes greater, since most of this equipment can cause major harm as well as provide adequate ventilation.

There are two basic types of mechanical ventilators: the pressure cycled and the volume cycled. Each has inherent assets and problems. The pressure cycled ventilator is generally operated from a compressed gas source and delivers to the patient varying mixtures of oxygen, depending upon the source gas and the pressure-flow relations of the machine and the patient's airways. This is a major problem with most pressure cycled ventilators. The concentrations of oxygen are unknown unless they are carefully measured and controlled. In addition, the pressure cycled ventilator cycles off when it arrives at a pressure set by the operator, thus tidal volumes can be greatly varied as lung compliance changes. Therefore, one must measure the oxygen delivery and tidal volume generated by such ventilators to provide adequate oxygenation and ventilation. The major assets of pressure cycled ventilators are that they are relatively inexpensive, small in size, and very versatile.

The volume ventilators, by contrast, deliver to the patient a controlled tidal volume, independent of the pressure required to generate such a volume. With constant volume delivery, minor variations in lung compliance and airways resistance are less likely to result in major ventilatory changes. Most volume ventilators have a device which directly controls oxygen delivery to the patient, or a system with a nomogram which allows one to arrive at the inspired oxygen percentage. However, there are some which require that oxygen percentage also be measured as in the pressure cycled ventilators.

It can be recognized that the primary factor in the proper use of mechanical ventilators is physician and/or inhalation therapist knowledge of a particular machine, and their ability to relate the patient to such a machine. In considering what a mechanical ventilator should do, the following equation demonstrates that to increase a patient's alveolar oxygen percentage, one can either increase the inspired oxygen percentage, decrease oxygen consumption, or increase alveolar ventilation.

$$F_{A_{O_2}} = F_{I_{O_2}} - \dot{V}_{O_2}/\dot{V}_A$$

$F_{A_{O_2}}$ = % alveolar O_2.
$F_{I_{O_2}}$ = % inspired O_2.
$\dot{V}_{O_2}$ = O_2 consumption.
$\dot{V}_A$ = effective alveolar ventilation.

Mechanical ventilators function in several ways to provide these changes. The inspired oxygen concentration can be controlled at any level necessary for a given patient. By assuming part of the work of breathing, mechanical ventilators will decrease oxygen consumption, particularly in those patients who have a remarkable increase in the work of breathing. Additionally, alveolar ventilation can be increased or decreased with a mechanical ventilator by adjusting the patient's tidal volume and/or respiratory rate. Since all of these factors are of direct importance in oxygenation, it is valuable to remember this equation. Also important to keep in mind is that the level of carbon dioxide tension is controlled by the level of alveolar ventilation. As alveolar ventilation is increased, carbon dioxide tension will be decreased and vice versa. (Since we are discussing the proper use of mechanical ventilators, I have chosen to disregard the use of ventilators for intermittent positive pressure breathing therapy.)

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In considering the mechanical ventilators, one must think of the indication for their use:

1. To substitute for the normal work of breathing.
2. To assume an increased work of breathing with increased airway or tissue resistance or increased dead space ventilation.
3. To change to a more effective pattern of ventilation.
4. To stabilize the chest wall after chest trauma.
5. To manage pulmonary congestion or edema.
6. To improve oxygenation when severe hypoxemia cannot be corrected by other means.

Although some of these indications might be better satisfied with a particular type of respirator, with proper knowledge and experience a pressure or volume cycled ventilator might reasonably well provide for any of these indications. This is a very important consideration as people become more and more dependent upon the more expensive volume cycled ventilators. It may be easier to manage a patient with multiple complications with these types of ventilators, however, it is in many circumstances unnecessary. Therefore, it is appropriate to contrast the complications which occur with these two types of ventilators.

Complications of Mechanical Ventilation

1. Problems of tubes or tracheostomies
2. Reduction of venous return
3. Atelectasis
4. Oxygen toxicity
5. Infection
6. Acid-base abnormalities
7. Gastrointestinal complications
8. Technical and mechanical complications
9. Emotional problems
10. Miscellaneous

Intubation of a major bronchus leading to atelectasis of the other lung, tube dislodgment, laryngeal damage or edema, or post-extubation laryngeal problems are well known to anesthesiologists. The tracheostomy avoids these problems which occur above the tracheostomy site; however, it contributes the additional problems of an open wound and a rigid tube through the neck, which might lead to bleeding, tracheostomy-site infection, or necrosis with erosion of vessels. Tracheal stenosis may follow either tracheostomy or indotracheal tube intubation. There is little difference in the frequency of these complications with a pressure or volume cycled ventilator.

Reduction in venous return resulting in decreased cardiac output, in our experience, has been much more commonly a problem in patients who are hypovolemic. Autonomic dysfunction and prolonged hypoxemia also are factors with this complication. To avoid this, one must monitor the blood pressure and urine output, and reduce mean inspiratory pressure, in addition to providing adequate fluid volume. This is probably the major indication for the use of a volume ventilator to deliver the tidal volume rapidly, particularly in patients with high compliance losses or high airway resistance. In these instances, a pressure cycled ventilator may require too long a time to provide an adequate inspiration maintaining a positive intrathoracic pressure for excessive periods. Most ventilators are fitted with a negative pressure device which operates during the end of exhalation to enhance venous return. This in our hands has been of little or no value and, at least in patients with chronic obstructive pulmonary disease, is relatively contraindicated since it produces closure of the poorly supported airways, leading to miliary atelectasis.

Atelectasis occurs in patients on prolonged mechanical ventilation, particularly in those with a high-inspired oxygen percentage. It may be manifested in numerous ways; however, typically it is indicated by an increase in oxygen requirement and decreasing compliance. Compliance loss is indicated by increasing inspiratory pressures to provide the same tidal volume or a decrease in tidal volume with a fixed inspiratory pressure. To avoid this problem, a proper respiratory pattern which provides for overall ventilation of the lungs must be established. Continuous positive pressure ventilation, inflation hold, and intermittent sighing are all approaches to this problem. Most volume ventilators have the ability to perform one or more of these functions. However, they can also be readily handled with a pressure cycled ventilator with proper inhalation therapy or nursing care to provide for intermittent deep breathing of patients and adequate airway toilet. A very important factor in prevention of atelectasis is adequate humidification of inspired gases. Chest physiotherapy, suction, and bronchoscopy are also helpful in the avoidance and treatment of this problem.

I would like to mention that oxygen toxicity usually occurs only with high-inspired oxygen percentages and it is greatly enhanced by prolonged

exposure. There are obviously multiple factors involved. It is of interest in our experience that if it does occur, it appears largely reversible if the patient survives. Particularly important to mention is that most all pressure cycled ventilators deliver higher oxygen concentrations than one would suspect. A common misconception is that on the air dilute setting these ventilators deliver 40% oxygen. Therefore, one must set up this type of respirator by measuring oxygen delivery to avoid oxygen toxicity. This is done either by operating the pressure cycled ventilator with compressed air and adding oxygen, or by adding compressed air to an oxygen-driven machine while monitoring inspired oxygen percentage. One must be aware that as the pattern of the patient's breathing changes, there will be varying percentages of oxygen delivered by these types of ventilators.

Infection is a major problem with mechanical ventilators since the warm, humid inspired gases, tubing, nebulizers, and humidifiers provide good culture media for many gram negative organisms. Mechanical ventilators have been found to be a source of gram negative infection in many hospitals. In our experience in culturing respirators, we have found that no respirator had organisms cultured from it prior to the organism being grown from the patient's sputum. Thus if respirator tubing is changed at least daily and sterilized properly prior to each use, the probability that these machines will result in spread of infection decreases. The practice of using a machine on more than one patient must be condemned unless everything from the respirator head out to the patient is changed between patients. Infection is managed with proper identification of the organism and specific therapy.

Inadequate humidification of inspired gases is one of the major problems in the use of mechanical ventilators. At room temperature (70°F), a gas saturated with water vapor contains approximately 20 mg of water per liter of gas. At body temperature, 44 mg of water are required to saturate a liter of gas. Since normal tracheal air is 100% humidified at body temperature, it is practically impossible to provide adequate quantities of water to equal the normal condition without passing the inspired gas mixture through a heated humidifier or nebulizer. This fact makes the use of heated humidifiers or nebulizers absolutely necessary with ventilators to avoid drying and damaging airway mucosa and obstruction of airways with inspissated secretions.

Most patients who have chronic respiratory failure will have a compensated respiratory acidosis. As carbon dioxide is removed with an efficient mechanical ventilator, severe post-hypercapneic metabolic alkalosis may be produced. The ability of dissolved carbon dioxide to traverse the blood brain barrier with great ease and the resistance of bicarbonate to cross the same barrier may result in central nervous system alkalosis if $PaCO_2$ is too rapidly reduced. This can lead to convulsions, coma, and death, and must be considered in all patients who are being placed on mechanical ventilators. For this reason, the arterial pH rather than the $PaCO_2$ should be the controlled variable. There is evidence to indicate that patients on mechanical ventilators will retain fluid, therefore, patients must be weighed daily and electrolytes must be measured frequently.

A significant number of gastrointestinal complications are seen in patients severely ill with respiratory failure. The most life threatening is gastrointestinal bleeding. This, while a significant problem, has not been too common in our experience. A more common problem is gastric distension or paralytic ileus in patients with severe lung disease. This may result in limitation of movement of the diaphram and a decrease in ventilation as well as basilar lung atelectasis.

Technical and mechanical problems must always be considered. The ventilator which becomes disconnected from a patient or malfunctions is of no value to the patient. Thus there must be a positive connection between the patient and the respirator for the machine to function properly. We have adopted the use of the Mörch tracheostomy tube and have had little difficulty with disconnection following this change. Since such problems may be life threatening and each type of respirator has a particular set of associated problems, the therapist or physician must be familiar with the problems which are possible with a particular type of ventilator. Changes in ventilatory or oxygen requirements must always be considered in managing patients on ventilators. Therefore one must measure these modalities frequently. Obviously, there are human errors in management and the scope of these is beyond this discussion.

The miscellaneous complications which occur are multiple. Major cardiovascular problems, such as arrhythmias, digitalis toxicity, and pulmonary emboli are not necessarily related to ventilators; however, they must be recognized in patients on ventilators. Pneumothorax and mediastinal emphysema

must be anticipated, since they may cause marked difficulty and frequently occur in ventilator patients.

The other major problem is weaning a patient from a ventilator. There are several factors to utilize in deciding when to begin weaning a patient:

1. Oxygen requirement: alveolar-arterial oxygen gradient should be less than 300 mm Hg breathing 100% O_2
2. Tidal volume: greater than 10 cc per kg body weight off respirator
3. Vital capacity: greater than twice the tidal volume
4. Ratio dead space to tidal volume (Vd per Vt): less than 0.5
5. Inspiratory negative pressure: more than 20 cm H_2O negative pressure

These are obviously not the only factors in weaning. The clinical judgment of the nurses and inhalation therapists is of major importance and is relied on heavily in our respiratory care unit. There are several problems which we routinely see in patients who are difficult to wean from respirators. The patient must be ready emotionally as well as physiologically to be removed from the respirator. He should have arterial blood gas values controlled near to those that he can support on his own without assisted ventilation. The patient should be cycling the ventilator himself; although this is unnecessary, it is helpful. Adequate humidification must be provided at all times when he is off the ventilator or he will have further problems with secretions and airway obstruction. His secretions should be under optimal control. One should begin with brief periods off the ventilator, that is, five to ten minutes per hour. Time off the ventilator is prolonged as the patient's tolerance increases. Even while the patient is off the ventilator, his lungs should be hyperexpanded frequently. Arterial blood gases, vital signs, and patient condition must be observed repeatedly during this period. We have always allowed the patient initially to sleep on the ventilator and be weaned only during the daytime; then he finally is allowed to sleep without ventilatory assistance. Another very important aspect of weaning the patient is emotional support. A patient who can communicate vocally has a much better opportunity for a reasonable emotional state. Our policy is to put in a lightweight plastic tracheostomy tube which can be plugged to allow the patient to talk while he is being weaned. This procedure in many circumstances has been of great value.

The proper use of mechanical ventilators is related to many problems; however, the primary one is the knowledge of the physician, nurse, inhalation therapist, and other paramedical personnel with a given ventilator. It is important to remember that there are certain inherent problems with all ventilators. These problems must be carefully searched for and avoided.

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Postoperative Ventilatory Care*

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Postoperative ventilatory care implies that some significant percentage of surgical patients cannot breathe adequately in the postsurgical state and need to be appropriately assisted in order to do so. It further implies that there may be some difficulty in or complication resulting from such care. Both implications are correct.

However, if we are to deal effectively with this problem, that is, if we are to correct some defect in a physiologic fashion, we must understand how postoperative ventilatory mechanisms and physiology are upset.

While many forces, both pre- and intra-operative, come to bear on the immediate postoperative ventilatory status of the patient, the common denominator in virtually all instances is hypoventilation. Unfortunately, for the patient's sake, this physiologic abnormality occurs at a time when normal protective reflexes and a fully alert state of consciousness are wanting. For some hours, or even days, the patient exists in a physiologic "twilight zone"—neither surgically anesthetized nor fully capable of protecting himself from his environment.

What causes this hypoventilation? Obviously, many factors related to both the anesthesia and the surgery are responsible.

Every known general anesthetic, barbiturate, narcotic, sedative, and tranquilizer is a central nervous system depressant, and in sufficient dose will depress ventilation. Muscle relaxants, which frequently produce a greater effect in the immediate postoperative period than we think they do, impair ventilation by their action. In addition, anesthesia even of relatively brief duration, predisposes toward the development of diffuse, generalized microatelectasis. A series of blood gas analysis routinely performed on young, healthy women immediately following elective uncomplicated D&C will soon convince even the most skeptical that something is amiss in the efficiency of breathing. Arterial oxygen tension in these circumstances is almost invariably depressed, even when the PCO_2 is normal. Now, add to this array of abnormalities the fact that some anesthetics produce a degree of metabolic acidemia, and that this in turn will adversely affect the metabolism and pharmacologic reversal of certain relaxants. The stage is now set for a potential disaster.

Next come the adverse effects of surgery. The immediate postoperative effects on pulmonary functions of elective upper abdominal surgery are typical. The patient is in pain; he splints; he typically breathes rapidly, but shallowly. He either cannot or will not take a deep breath, and therefore, cannot cough effectively. Secretions tend to accumulate, and we have another reason to develop atelectasis.

The upper abdominal procedure is more depressant to the postoperative vital capacity than the lower abdominal operation. Non-abdominal (and non-thoracic) procedures are not associated with any significant change in pulmonary function related to the surgery per se.

The type of anesthesia, whether conduction or general, has considerably less influence on the adequacy of postoperative coughing ability than does the anatomic site of surgery. Upper abdominal operations are in fact slightly more debilitating in this regard than are intrathoracic procedures, so long as actual lung tissue is not excised.

The highest incidence of postoperative pulmonary complications occurs in elderly patients, as might be expected. Even though these data are 25 years old, the situation has not changed markedly as far as the upper-age groups are concerned. Postoperative pulmonary complications are also more

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likely to occur in obese patients, in chronic cigarette smokers, and (although not agreed upon by all investigators) seem to increase as the duration of anesthesia and surgery increase. Needless to say, the existence of significant preexisting pulmonary disease raises the probability of postoperative problems.

Preoperative abnormalities in vital capacity and the FEV_1 are related to the operative risk. When the preoperative vital capacity is less than 80% of the predicted, or when the FEV_1 is less than 60% of the total vital capacity, or especially when both of these abnormalities coexist, the risk of surgery and anesthesia, particularly surgery of the upper abdomen, increases tremendously.

Let us consider an example which is not unusual and, indeed, is being seen more and more frequently by those of us with a busy clinical practice. A 50-year-old, 210-pound male, who has smoked a pack and a half of cigarettes a day for 25 years comes in for elective vagotomy and pyloroplasty. After three hours of nitrous oxide, oxygen, halothane, and curare relaxation he arrives in the recovery ward. His tidal volume is 350 ml, his vital capacity is 600 ml, his PaO_2 is 53, his $PaCO_2$ is 49, and his pH is 7.29.

Let us be sure that we delineate the problem accurately: The question is not, "Will this patient develop significant hypoventilation and, finally, respiratory failure?" The question is, "When?" He is already seriously hypoventilating, is hypoxemic, and is developing a respiratory acidemia. He is overweight and probably has significant chronic bronchitis. All too frequently, we see this patient who becomes febrile within 24 hours of surgery and develops pneumonia. His hospitalization is prolonged, his convalescence complicated, and he has inherited an increased risk of mortality. He has joined that ever growing group of patients who share the most common of all postoperative problems—pulmonary complications.

Knowing that anesthesia may impair ventilation, knowing that surgery adds insult on top of injury to the breathing mechanism, and knowing that preexisting lung disease adds two strikes before surgery is even contemplated, one cannot escape the clear indication for prophylaxis. Indeed, the hallmark of postoperative ventilatory care is preoperative pulmonary preparation. It is now clearly demonstrated that appropriate pre-, intra- and postoperative care of patients with chronic pulmonary disease can result in morbidity and mortality rates similar to those in patients with no pulmonary disease, treated in the usual fashion, that is, largely ignoring the pulmonary system unless complications occur.

Preoperative pulmonary preparation requires that someone, usually the operating surgeon or the initial referring physician, be aware that the patient has some respiratory difficulty, either potential or existent, and that this difficulty poses a threat to his postsurgical survival. With this in mind, the following preoperative program is suggested:

Which diseases or symptoms should concern us?

a) Acute respiratory infection obviously should be eliminated prior to elective surgery. In the emergency case we have to go ahead with anesthesia and surgery, and this is acceptable, but it increases the risk for the patient. Otherwise elective surgery should be postponed.

b) Chronic bronchitis—a history of cigarette smoking, cough with production of sputum, especially purulent sputum, is enough to make the diagnosis of this disease.

c) Emphysema—this disease cannot be cured or even reversed to any great extent, but it is often associated with considerable bronchial spasm and/or infection, both of which should be eliminated or decreased in severity prior to anesthesia.

d) Asthma—we are concerned here with the patient who is actually wheezing with dyspnea. These patients should be rendered symptom-free prior to elective surgery if at all possible.

e) Bronchiectasis—these patients always produce sputum. They must be able to cough and hopefully should not get superinfection.

f) Dyspnea as a symptom should never be ignored. Its origin may be either respiratory or cardiovascular. The system which is responsible for its genesis should be determined and evaluated as to the actual diseases present. This is obviously easier said than done, but in the presence of uncompensated heart failure, vigorous diuresis is a relatively benign yet fairly effective way to improve this situation.

How do you diagnose these diseases? The points in physical and clinical diagnosis are not needed in this discussion as they are no doubt

well appreciated by all of us. What is needed, I think, is one simple reminder. We must consider smouldering, lingering, or occult pulmonary disease in each patient we contemplate sending to surgery. We must suspect it and look for it, otherwise somebody will develop a serious pulmonary complication or perhaps die in the postoperative period—somebody who would otherwise return to some years of further productive life. The presence of cough with yellowish or greenish sputum regardless of how scant in quantity, means pulmonary infection, bronchitis probably, but perhaps bronchiectasis.

"All that wheezes is not asthma," is sound albeit aged advice. On the other hand, wheezing should suggest asthma since this disease cannot exist without this sign.

Obstructive airways disease carries greater postoperative morbidity than does restrictive disease due to the limited ability of effective coughing. A quick, fairly reliable, and quite unsophisticated qualitative appraisal of airway obstruction is the match test. The one-second and 0.5-second FEV_1, or timed vital capacity, is obviously more accurate. A point to remember is this: Severe emphysema and bronchitis can exist in the presence of a normal chest x-ray and with no increase in anterior-posterior diameter of the chest. Do not rely on these signs as the tip-off to the presence of pulmonary disease.

The relationship of pulmonary function tests and arterial blood gases to postoperative prognosis. Pulmonary function studies such as vital capacity, timed vital capacity, and maximum mid-expiratory flow rate are sensitive but not specific tests (they may be abnormal in all who do poorly postoperatively, but they also may be abnormal in those who do well). The $PaCO_2$ is quite specific but not particularly sensitive as it invariably predicts postoperative difficulty if elevated preoperatively. But the patients with this abnormal test in the preoperative period are very few of all those who are operated upon. Both the pulmonary function test plus the blood gas analysis and the response of both of these to preoperative respiratory preparation are the best indication of the postoperative course and the patient's tolerance of surgery and anesthesia.

How do we prepare the patient for surgery? Once the diagnosis of plumonary disease is made and some quantification of this function is achieved, our entire efforts are aimed toward one simple goal—getting the patient in as good a shape as possible before surgery. Regardless of the severity of his pulmonary disease we should be satisfied that he can be improved no further before elective surgery and anesthesia is undertaken. This includes:

a) the eradication of acute infection
b) the control of chronic infection
c) the relief of bronchial spasm
d) an improvement in the sputum clearance and bronchial drainage
e) the reversal of uncompensated congestive heart failure on the basis of corpulmonale, if such is present.
f) all steps to improve muscular power for coughing and deep breathing (nutrition, electrolytes, and humidification of airway)
g) a familiarization with inhalation therapy equipment likely to be used in the postoperative period, ventilators, etc.
h) a familiarization with chest physiotherapy techniques for effective coughing, sputum production, and exercises.

Even if all this produces little detectable improvement in the patient, we have the advantage of knowing that his disease is largely irreversible and that his tolerance for extensive surgery and prolonged anesthesia will be minimal.

What is the best anesthetic technique or agent? It has been repeatedly demonstrated that the drug used or the technique employed in producing anesthesia for such patients is of considerably less importance than is the skill with which the particular drug or technique is applied. In other words, the anesthetic is not what is important, it is the anesthesiologist.

What are the details of postoperative care? This is a continuation of the preoperative regime, that is:

a) awareness of the possibility of complications and actively looking for them.
b) maintenance of adequate alveolar ventilation (as determined by arterial blood gases) without excessive energy expenditure (measurement of tidal volume, vital capacity, minute ventilation, and frequency of ventilation).
c) maintenance of an unobstructed airway. An endotracheal tube may be used in these circumstances if needed.
d) meticulous STERILE tracheobronchial suction as necessary.
e) *effective* humidification—both in the airway and parenterally.

f) frequent chest physiotherapy to help in coughing, deep breathing, and secretion removal.

g) establishment of assisted ventilation if pulmonary function tests and arterial blood gases deteriorate beyond a certain point, or if one has reason to *think* that they will deteriorate beyond a certain point, that is, a $PaCO_2$ above 50, a PaO_2 below 200 on 100% oxygen, a tidal volume less than 3 ml per kg, a vital capacity less than 10 ml per kg, or a respiratory frequency of greater than 35 per minutes in adults.

If the possibility of preoperative pulmonary disease is suspected; if it is diligently sought for; if a degree of functional impairment as well as pathologic diagnosis is established; and if the patient is rendered as symptom-free as possible with respect to infection, sputum clearance, ability to cough, and freedom from bronchial spasm, he will tolerate his surgery and anesthesia as well as modern medical care can allow him to. And if postoperative ventilatory care is necessary, it will be anticipated and utilized appropriately.

Pulmonary Function Testing for Preoperative Study of Patients for Anesthesia and Surgery*

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Pulmonary complications are the most prevalent causes of morbidity and mortality in patients who undergo surgical procedures. Simple pulmonary function tests which can detect pulmonary dysfunction may be performed preoperatively. If proper measures are taken (chest physiotherapy, postural drainage, bronchodilating agents, antibiotics, humidification of inspired gases, cessation of cigarette smoking), morbidity and mortality can be reduced significantly.

Pulmonary function tests are especially important in patients with borderline pulmonary reserve who need major surgery. After objective evaluation, the anesthesiologist and the surgeon can provide better care for the patient. These studies may also suggest the patients who are more likely to develop postoperative complications.

In many patients, a thorough medical history and physical examination, in addition to a complete blood count with differential, urinalysis, electrolytes, BUN, and chest x-ray, often will give satisfactory information, and many patients will not need pulmonary function testing prior to anesthesia and surgery.

Should history and physical examination show that pulmonary function tests are indicated, they will also indicate the type of tests to be carried out. A history of chronic productive cough, dyspnea, pleuritic chest pain, occupational respiratory hazards, frequent past episodes of pneumonia, pleurisy, chest colds, and sudden reduction in strength should strongly suggest possible pulmonary dysfunction.

Findings on examination of the chest such as prolonged expiration, diffuse or localized wheezing, absent breath sounds, rales, chest-wall deformities and scars, hypertrophy of scalene muscles, and pulmonary osteoarthropathy again should suggest possible abnormalities in lung function, and proper pulmonary function tests should be performed.

There are a variety of pulmonary function tests which may be used to detect dysfunction. In general, they can be divided into two groups:

1. Those relating to the ventilatory function of the lungs and thoracic wall.
2. Those relating to pulmonary gas exchange.

Ventilatory Function Tests. Ventilatory function is determined by measurement of static lung volumes. These are somewhat indicative of the elastic resistance of the lungs and chest wall and dynamic lung compartments; these tests are mainly a reflection of nonelasticity.

Static Lung Volumes. Static lung volumes are assessed by measuring the vital capacity which changes according to height, age, and sex. Full cooperation of the patient during the procedure is essential. Integrity of the entire respiratory system (respiratory centers, thorax, the connections between these two, chest wall, pleura, lung paranchyma, and airways) is necessary for normal vital capacity.

If a person has less than predicted normal vital capacity, by definition he has restrictive lung disease. Normal values range $\pm 15\%$ of the predicted. As an isolated test, vital capacity is of limited clinical value in differential diagnosis of diseases of the chest. However, serial measurements of vital capacity may be helpful in assessing the degree of improvement or worsening in certain conditions such as neuromuscular disorders, or diffuse interstitial pulmonary fibrosis.

Dynamic Lung Volumes. More important information could be obtained by measuring timed vital capacity or forced vital capacity. A young or middle-aged normal person should be able to exhale 80% of his vital capacity in one second and 97% in three seconds. If the ratio between one-

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second forced expiratory volume ($FEV_{1.0}$), over forced vital capacity (FVC) is less than 80%, he is considered to have obstructive lung disease. Diminution in $FEV_{1.0}$ to a liter or less indicates severe impairment of ventilatory function and a somewhat poor surgical risk.

Expiratory flow rates can be determined at different points during forced expiratory curve. The forces tending to reduce the size of airways (peribronchial pressure and the force generated by constriction of bronchiol muscles) are balanced by those attempting to increase the size of airways (intraluminal pressure and radial traction of elastic fibers). During forced exhalation, the alveolar pressure and the intrathoracic pressure are greater than atmospheric pressure. The intramural pressure decreases gradually from peripheral airways to atmospheric pressure at the airway opening. At some distance in the airway, intraluminal and pleural pressures are equal. This is called the point of equal pressures. Beyond this point, intraluminal pressure is less than pleural pressure; this would tend to narrow airways, thus limiting flow.

In patients with altered and more collapsible airways, flow is limited at lower levels of pleural pressure. The maximal flow rate produced by forced exhalation depends upon the level of lung inflation. At maximum lung inflation, expiratory flow increases as the pressure increases. At lower lung volumes, expiratory flow increases as pressure increases up to a certain level, after which more effort cannot increase and may even decrease flow rate. This explains why the maximum mid-expiratory flow rate (MMFR or FEF 25%–75%) is the most sensitive test for expiratory flow rate determination since the initial 25% of the FVC is primarily effort-dependent and the last 25% affected by diminished lung volumes.

The MMFR measures the maximum rate of flow in the mid portion of FVC curve (FEF 25%–75%). (The length of time necessary to exhale the middle 50% of the forced vital capacity is measured and flow rate is calculated.) Normal values are 3–4.5L per second. It should be emphasized that small airways (2 mm in diameter) are only responsible for approximately 15%–20% of the total airway resistance, so marked increases in peripheral or small airways will not be detected by the conventional tests such as $FEV_{1.0}$ or MMFR.

In the early stages of chronic bronchitis, pulmonary emphysema, and bronchiectasis there is a significant degree of involvement of the small airways. In the early stages of these conditions, frequency-dependent dynamic compliance and alveolar arterial oxygen tension gradient, A-a PO_2, may detect pulmonary dysfunction. For clinical purposes, however, simple spirometric studies with measurements of FVC, $FEV_{1.0}$, and MMFR are satisfactory. Improvements in flow rates after administration of bronchodilating agents suggest the presence of partially reversible obstruction. One-second forced expiratory volume $\times$ 30 gives indirect measurement of maximum voluntary ventilation (MVV).

If a bedside study of ventilatory function is desired, a Wright Respirometer may be used for measuring tidal volume and inspiratory capacity. A Peak Flow Meter may also be used for measuring peak flow rates.

Failure to blow out a lighted match held six inches away from the wide-open mouth again suggests significant reduction in flow rates.

In general, patients with obstructive lung disease are more prone to develop postoperative pulmonary complications such as atelectasis and broncho-pneumonia. This is why pulmonary function testing is important for determining the type of physiologic abnormality present so that proper measures can be taken to improve potentially reversible abnormalities.

Pulmonary Gas Exchange. One of the most important functions of the lungs is alveolar gas exchange which involves the following processes:

1. Ventilation
2. Uniform distribution of inspired air
3. Diffusion
4. Pulmonary capillary blood flow

Normal alveolar gas exchange maintains partial pressures of oxygen and carbon dioxide in the arterial blood within normal limits not only at rest, but also during increased physical activity and body metabolism. Abnormality in any of the above processes or in any combinations of the four, results in hypoxemia or hypoxemia and hypercapnia if the person is breathing room air.

Arterial gas studies indicate:

1. The level of oxygenation (PO_2 in mm of Hg)
2. The level of ventilation (PCO_2 in mm of Hg.)
3. The hydrogen ion activity (pH)

The above determinations are extremely important in all seriously ill patients.

It is often impossible to judge the levels of ventilation and oxygenation by clinical evaluation alone. There is much overlapping between signs and symptoms related to hypoxemia and hypercapnia: nervousness, headache, irritability, confusion, coma, altered blood pressure, tachycardia, etc. Sometimes signs and symptoms related to hypoxemia and hypercapnia are absent and only by measurements of arterial gas studies can the level of ventilation and oxygenation be determined and appropriate treatment initiated.

An A-a PO_2 gradient greater than 10 mm Hg on room-air breathing indicates a defect in blood gas equilibrium. The three primary mechanisms of increased A-a PO_2 gradient are impaired diffusion, venous-to-arterial shunting of blood, and abnormal ventilation/perfusion ratios in the lung.

The amount of true venous-to-arterial shunt is determined by having the person breathe 100% oxygen for 15 to 20 minutes. Normally, arterial PO_2 will increase to about 600 mm Hg. The observation of increased A-a PO_2 gradient on breathing room air and of a PO_2 greater than 550 mm Hg while breathing oxygen indicates that mismatching of the distribution of ventilation and perfusion in the lungs is the cause of hypoxemia.

The observation of high A-a PO_2 gradient on room air in the presence of normal spirometric studies may also suggest peripheral airway disease.

Whenever possible, arterial blood gas studies should be obtained at rest, after exercise, and sometimes after the administration of 100% oxygen for 15 to 20 minutes. The above studies may give valuable information in the evaluation and follow-up of patients with respiratory disease.

Normal arterial blood O_2 at sea level is found in two forms:

1. Dissolved O_2 (0.3 ml per 100 ml per 100 mm Hg)
2. Oxyhemoglobin (Hb O_2 19.7 ml per 100 ml)

Normally, the total O_2 content of arterial blood is approximately 20 ml per 100 ml. The amount of dissolved O_2 present is linearly related to arterial O_2 tension. If partial pressure of O_2 in arterial blood is 600 mm Hg, there is approximately 1.8 ml of physically dissolved O_2 per 100 ml blood.

On the other hand, the relation between oxyhemoglobin and partial pressure of O_2 is S-shaped. If PO_2 is 100 mm Hg, oxygen saturation is 96% to 98%. If PO_2 is 60 mm Hg, oxygen saturation is approximately 90%. In the flat portion of this curve, a large decrease in O_2 tension causes only a small drop in oxygen saturation. However, at the steep portion of this curve, a small reduction in O_2 tension causes a large diminution of O_2 saturation.

For instance, a drop of O_2 tension from 40 mm Hg to 27 mm Hg causes a reduction of saturation or O_2 content of approximately 25%. A high CO_2 tension and increased H^+ ion activity shifts this curve to the right. This is called the Bohr effect. Increased temperature and increased 2–3 DPG (2–3 Diphosphoglycerate) of the red blood cells can also shift this curve to the right. A low PCO_2, a high pH, a low temperature, and a low 2–3 DPG causes a shift to the left. Normally, a shift to the left in the lungs helps the loading of O_2 with hemoglobin. A shift to the right at tissue levels helps unloading of O_2 to tissues.

There are four causes of hypoxemia on breathing ambient air at sea level:

1. Uneven $\dot{V}/\dot{Q}$
2. Venous-to-arterial shunt
3. Alveolar hypoventilation
4. Impaired diffusion

In clinical medicine, uneven $\dot{V}/\dot{Q}$ is the most common cause of hypoxemia. However, in a given case, there is more than one factor responsible for hypoxemia.

Arterial PCO_2 indicates the balance between CO_2 produced at the tissue level and CO_2 eliminated by alveolar ventilation.

$$PaCO_2 \propto \frac{\dot{V}CO_2}{\dot{V}A}$$

Normally, alveolar ventilation is proportional to CO_2 production which is related to the rate of metabolism. In any given person at any given time, CO_2 production is at a certain level and only alveolar ventilation could change arterial PCO_2. In conclusion, we can say that the level of PCO_2 indicates the level of ventilation.

Hydrogen ion activity is determined by measurement of pH. According to the Henderson-Hasselbalch equation:

$$pH = PK^1 + \log \frac{(HCO_3)}{PCO_2 \times 0.03}$$

$$pH = 6.1 + \log \frac{24}{1.2}$$

$$pH = 6.1 + \log \frac{20}{1}$$

$$pH = 6.1 + 1.3 = 7.40$$

The ratio of HCO_3 and dissolved CO_2 determine the pH. As long as this ratio is 20, the pH should be normal.

There are four primary or simple acid-base disturbances as well as combined or mixed acid-base disturbances. Primary increase or decrease in PCO_2 indicates respiratory acidosis or alkalosis respectively. Primary increase or decrease in HCO_3 indicates metabolic alkalosis or acidosis respectively.

The following are some indications for pulmonary function testing:

1. To determine the type of physiologic alteration present.
2. To quantitate the degree of functional impairment.
3. To initiate therapy on a more rational physiological basis and objectively follow the efficacy of therapy.
4. Preoperative risks evaluation. Re: anesthesia and surgery.

The following arterial gas studies were obtained on room air in a 60-year-old man with chronic obstructive pulmonary disease (COPD):

PO_2:60 mm Hg

PCO_2:55 mm Hg

pH:7.34

HCO_3:30 m Eq/L

The above studies indicate mild hypoxemia and partially compensated respiratory acidosis.

Spirometric studies revealed moderately severe airway obstructive disease. One day after admission, elective cholecystectomy was performed. One day after surgery, arterial gas studies on ambient air were obtained.

PO_2:45 mm Hg

PCO_2:80 mm Hg

pH:7.26

HCO_3:35 m Eq/L

The above studies indicate severe hypoxemia and partially compensated severe respiratory acidosis. It took approximately 12 days to correct arterial gas studies and acid-base disturbance.

On the other hand, in another patient with COPD and more or less the same arterial gas abnormalities, elective gall bladder surgery was postponed for seven days and the patient was given chest physiotherapy, postural drainage, bronchodilating agents, antibiotics, and humidified inspired air. He stopped smoking. Postoperative status was entirely unremarkable.

In conclusion, if history and physical examination indicate pulmonary dysfunction, simple pulmonary function tests should be obtained and proper measures taken to reduce morbidity and mortality in surgery patients, especially those with underlying chronic lung disease.

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Body Temperature During Surgery and Anesthesia*

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The recognition of fulminant hyperthermia and accidental hypothermia during anesthesia and surgery has given a new impetus to clinical thermometry in the operating room. It is suggested that in order to recognize and avoid these conditions in the anesthetized patient, a routine of continuous monitoring of body temperature be added to our armamentarium for patient care.

One of the problems that has to be solved is the standardization and selection of a physiologically meaningful site for the monitoring of body temperature. In order to select such a proper site, a brief discussion of functional anatomy and physiology of body temperature is here presented, together with a discussion of the advantages and disadvantages of the traditional sites, placing emphasis on a new site—namely the tympanic membrane.

The relative constancy of body temperature was recognized by Claude Bernard as a part of the regulation of the "milieu intérieur" required for the health and proper functioning of the cellular elements of warm-blooded animals. The healthy man does not exist with internal body temperature much outside the normal range of 36°-38°C, although during hard work and in febrile diseases he may tolerate for short periods of time temperature as high as 40°-41°C. Denaturation of vital cellular proteins occur above 44°C. Man may tolerate hypothermic states for short periods of time during which his body temperature is as low as 27°-29°C, but these temperatures are incompatible with life except under the most careful medical supervision and even then not for periods longer than a few days.

The center for regulation of body temperature is in the hypothalamus (fig. 1). In this area two regions, anterior and posterior hypothalamus, have been recognized. The anterior region, also known as the "heat disposal" region in the event of total body heat gain, is involved in the initiation of thermoregulatory reflexes. These reflexes will activate the cardiovascular and respiratory system, cutaneous blood vessels, and sweat glands through the autonomic nervous system to help balance body heat through heat loss.

Cold stimulates the central nervous system in the posterior hypothalamus and the endocrine system through the pituitary gland. Its primary action on the periphery is to stimulate sensations of cold and possibly other cutaneous nerve endings which send thermoregulatory signals to the "temperature maintenance region." The posterior region of the hypothalamus, on receiving "cold signals" through the "shivering center," will activate the shivering reflex which is one of the most powerful physiological actions of the body in the production of heat.

Hormonal action of cold takes place through the hypothalamus. By lowering the temperature of blood going to the brain, cold stimulates the hypothalamus, which in turn affects the pituitary and the release of thyroid stimulating hormone (TSH) and adrenocorticotropic hormone (ACTH). These two hormones promptly act on their target organs to release thyrotropic and adrenal hormones which serve to increase heat production in the body tissue (fig. 1 and fig. 2). These hormones also serve to potentiate the direct effect of cold in producing extra body heat by shivering. There are interactions of the various endocrine glands on each other, and thus it is not easy to obtain a clear evaluation of the part played by a single glandular component (fig. 2).

Monoamines in the hypothalamus act as mediators of temperature response. Local infusion of 5-hydroxytryptamine have been shown to raise tem-

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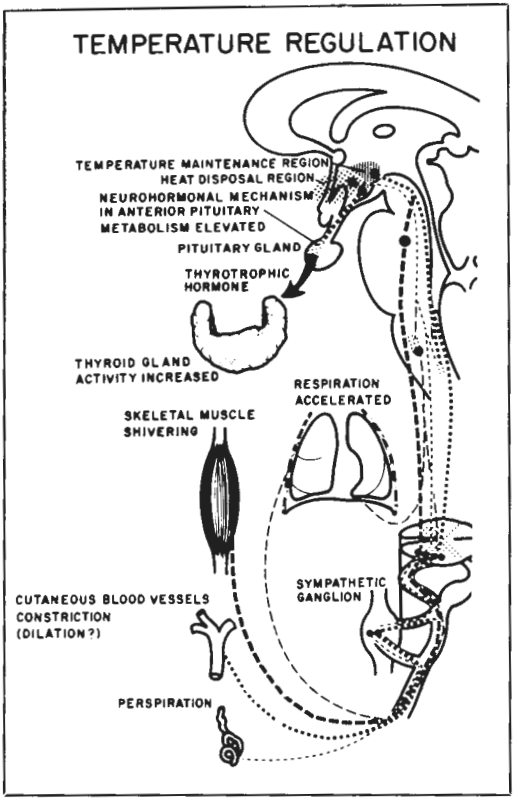

Fig. 1—Functional anatomy of physiologic temperature regulation.

perature in cats. It is suggested that the release of monoamines and their relative local concentrations act on the temperature cells of the anterior hypothalamus. Norepinephrine and epinephrine are concerned with regulating heat loss, and 5-hydroxytryptamine is involved with heat production.

In fever, in response to leukocyte pyrogens, the pyrogens act directly on the cells of the anterior hypothalamus. The magnitude of skin temperature appears of little importance in the regulation of body temperature. Logically, it makes the most sense to have the sensor for warmth inside the core of the body where the heat-generating metabolic activity originates, and the sensor for cold on the outside where the cold environment is located.

"Human Thermostat." Theodor H. Benzinger has proposed the concept of a "human thermostat" or a "temperature eye" being located in the hypothalamus. The temperature eye will sense the body temperature, as the retina of the eye is capable of sensing light. The set point, 37°C, of the human thermostat is located in the hypothalamus area.

The shifting of the set point from 37°C will cause the activation of thermoregulatory reflexes and, in effect, create the constancy of body temperature. Anesthetic agents, by depression of the hypothalamus, can cause lowering of the set point. The same effect has been attributed to aspirin, while it has been postulated that pyrogene will raise the set point of the human thermostat. Considering the functional anatomy and central regulation of body temperature, it becomes apparent that the logical site to monitor the central temperature is located in the cranium.

Rectal Temperature. The most widely used rectal temperature has been highly criticized for not being a true representative of core temperature. In monitoring of rectal temperature, one has to realize that this area does not have any thermal significance of its own. There are no thermoreceptive elements in the rectum. It is far away from the central nervous system and does not have direct relationship with the crossroad of circulation, that is, heart and great vessels. Sir George Pickering has observed "no clear relationship between changes in rectal temperature and changes in vasomotor tone."

The reliance on rectal temperature for the last hundred years has been responsible for the failure of clinicians to recognize and use the concept of central thermoreception in clinical thermometry. Our measurements at the Medical College of Virginia and the measurements of others in the anesthetized patient have shown that rectal temperature deviates widely from tympanic (central) measurements. Be-

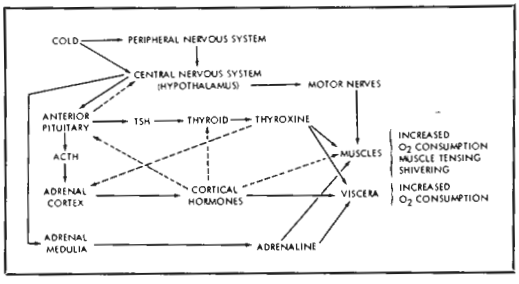

Fig. 2—Flow diagram of hormonal response to cold. (Reprinted with permission from Masson et Cie [éds.] *Les Concepts de Claude Bernard Sur Le Milieu Intérieur*, Paris: Libraires de L'Académie de Médecine, 1967, and from T. H. Benzinger.)

cause of these anatomical and physiological aspects of the rectum, such deviations make it nonrepresentative of core body temperature.

Esophageal Temperature. As will be discussed further, esophageal temperature in the anesthetized patient who does not experience sudden heat loss or heat gain somewhat represents core temperature in reference to central temperature. However, one has to realize, as J. D. Whitby and L. S. Dunkin have shown, that the esophageal temperature recorded in the anesthetized and intubated patient depends on the site of the esophagus at which it is taken. The longitudinal variation is greater than the lateral and can be by as much as 6°C. The lowest temperatures are found in the upper and middle third of the esophagus. Both longitudinal and lateral variations level out in the lower third. The lower fourth of the esophagus is both the warmest and the most stable. To reach this area, thermocouple leads should be inserted 45 cm from the nostril. This area is situated in the lower mediastinum below the pulmonary vein and between the heart and the descending part of the aorta. Carlsten and Crimley have shown that the esophageal temperature closely follows the temperature of intracardiac blood.

Tympanic Temperature. The tympanic membrane temperature, because of its proximity and similar blood supply, is very close to the central temperature. By placing a thermocouple in juxtaposition to the tympanic membrane, T. H. Benzinger has shown that its temperature accurately reflects the temperature of blood coursing through the brain (fig. 3). With the use of gradiant calorimetry, he has demonstrated that the changes in tympanic temperature are concordant with one of the thermoregulatory reflexes, namely the sweat rate, whereas skin temperature changes do not reflect sweat rate and are paradoxical and discordant.

Figure 4a, from Benzinger's study shows that when some subjects swallowed ice, cranial temperature decreased. At the same time, the sweat rate showed a parallel heat loss which was repeatedly constant.

Figure 4b shows the same subjects. When they swallowed ice, their skin temperature increased while at the same time their sweat rate, or heat loss, decreased (discordant relationship).

Clinical Thermometry in the Operating Room. In a group of about 30 patients (mostly adult) undergoing general anesthesia and surgery, continuous body temperature measurement was made from a thermocouple placed against the tympanic membrane. This source was compared with continuous and simultaneous measurements from the esophagus and rectum. The period of comparison ranged from 1.5 hours to 12 hours, depending on the length of the operation, and the time the patient spent in the recovery room. For the rectum and the esophagus, a soft plastic probe without cotton cover was used. For the tympanic membrane, a probe with a special "Q-tip" was used.

Each thermocouple was connected to a monitoring recorder, and three temperatures being monitored were transcribed directly to a Leeds and Northrup Company, Speedomax continuous writer.[1]

Fig. 3—Tympanic thermometer consisting of disposable thermocouple introduced into external auditory conduit. (Reprinted with permission from *Bild Der Wissenschaft*, Volume Three, July, 1964, and from T. H. Benzinger.)

[1] We would like to thank Leeds and Northrup Company for providing the monitoring equipment, and also acknowledge the support of Dr. John L. Patterson, Jr., Director, Cardiopulmonary Labs and Research, and Dr. C. Paul Boyan, Chairman, Department of Anesthesiology.

Figure 5 shows simultaneous monitoring of rectal, esophageal, and tympanic temperature in a patient during open heart surgery. Immediately after the bypass there is a profound fall in body temperature. (From a tympanic temperature of 37°C to 32°C). This has prompted some clinicians to advocate this technique in patients with fulminant hyperthermia to lower the body temperature. Figure 5 also shows the deviations of rectal temperature from tympanic and esophageal under the conditions of extracor-

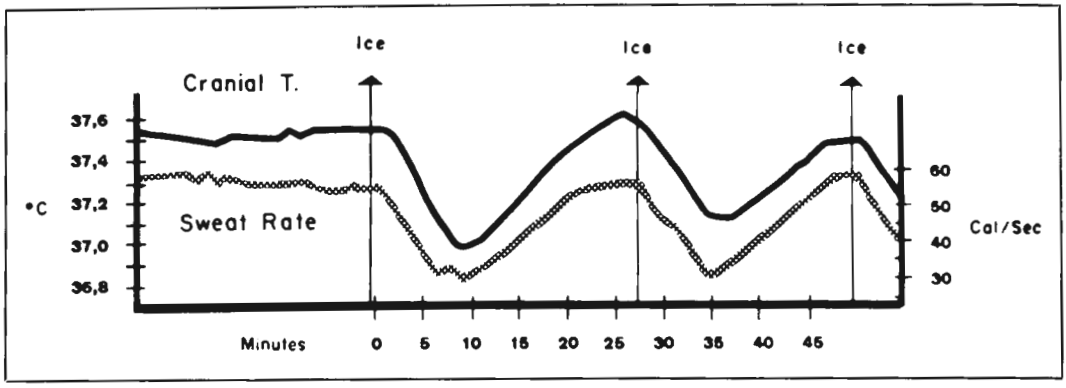

Fig. 4a—Concordant patterns of sweating rate and cranial (tympanic) temperatures observed during repeated oral ingestion of ice. (Reprinted with permission from Masson et Cie [éds.] *Les Concepts de Claude Bernard Sur Le Milieu Intérieur*, Paris: Libraires de L'Académie de Médecine, 1967, and from T. H. Benzinger.)

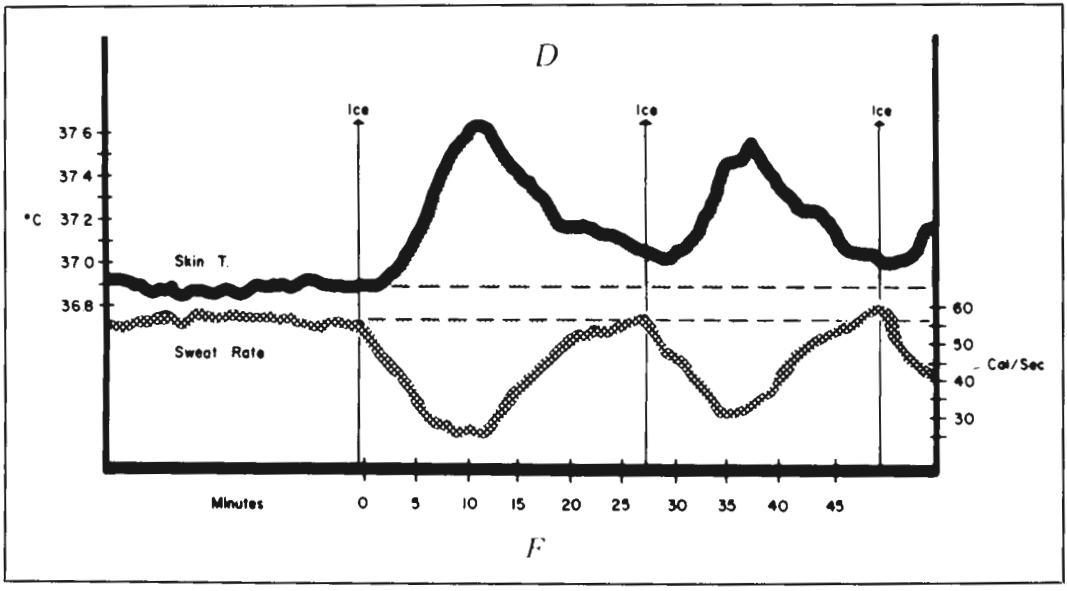

Fig. 4b—Discordant patterns of sweating and skin temperatures observed during repeated oral ingestion of ice. (Reprinted with permission from Masson et Cie [éds.] *Les Concepts de Claude Bernard Sur Le Milieu Intérieur*, Paris: Libraires de L'Académie de Médecine, 1967, and from T. H. Benzinger.)

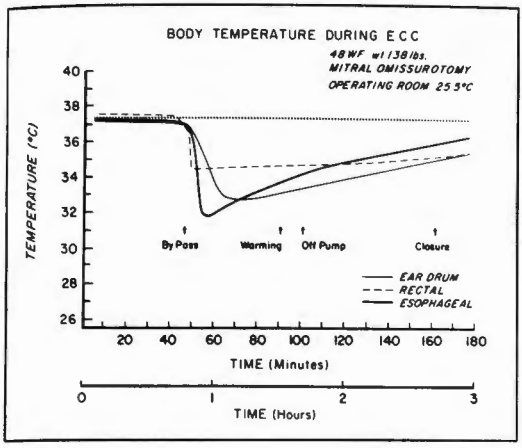

Fig. 5—Simultaneous monitoring of rectal, esophageal, and tympanic temperatures on a patient undergoing open heart surgery.

poreal circulation. It represents the fact that myocardial temperature, which is more in line with tympanic and esophageal temperature, can be much lower than rectal temperature at the termination of the by-pass. It also demonstrates that sole reliance on rectal temperature will result in not recognizing the cold myocardium, and this may contribute to the difficulty in recovery of the heart during open heart surgery.

Figure 6 shows another example of a patient undergoing open heart surgery with multiple "crash cooling" and "rewarming" periods during extracorporeal circulation. A similar deviation between rectal and esophageal, and tympanic temperature is noticed.

Figure 7 shows the rewarming period and accidental overheating of a patient under extracorporeal circulation with multiple "crash cooling" periods. It can be seen that in case of accidental overheating, the deviations between different sites of temperature discussed in figure 5 can exist.

Hypothermia During Anesthesia and Surgery. During clinical thermometry we noticed, as others have, that under modern operating room conditions (humidity of about 50% and temperature between 68°F and 75°F) the majority of patients undergoing different types of surgery had some degrees of fall in body temperature. Depending on the type and length of the operation, some patients could develop profound hypothermia.

Man being a homothermic animal has the ability to maintain his normal body temperature regardless of environmental temperature. An anesthetized man loses this ability. He becomes somewhat

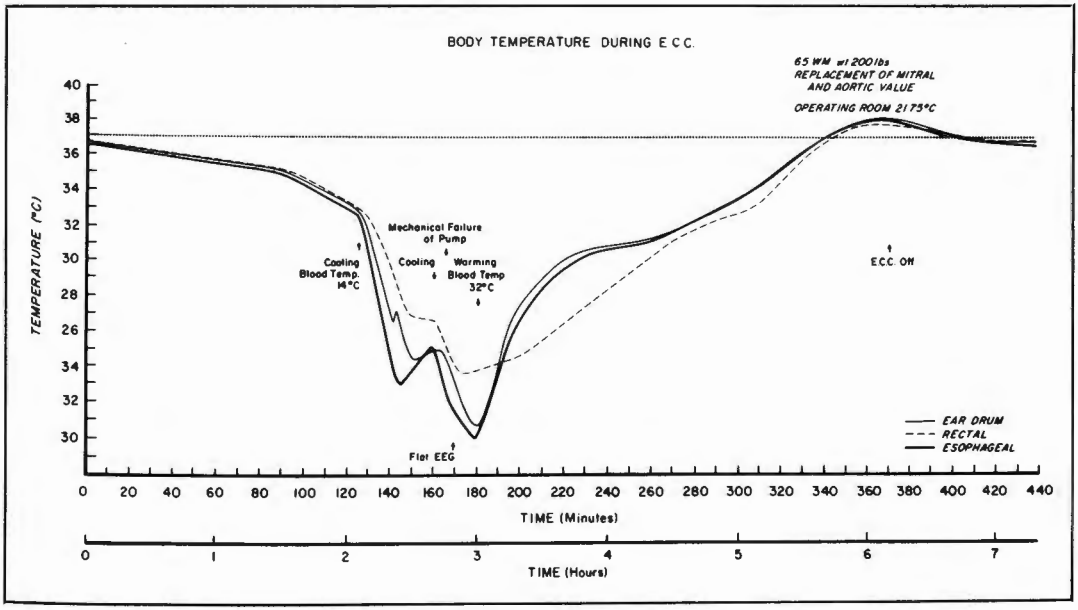

Fig. 6—Body temperature during extracorporeal circulation, multiple crash cooling.

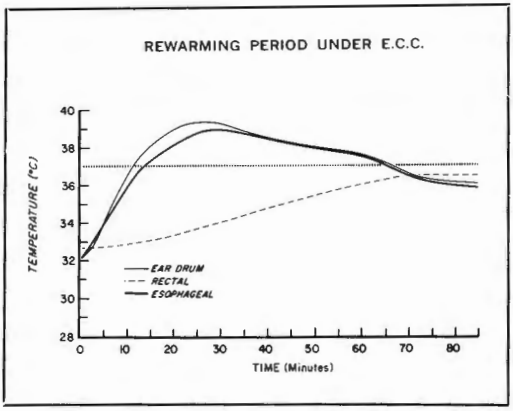

Fig. 7—Rewarming period under extracorporeal circulation, overheating by heat exchanger.

poikiothermic and follows the environmental temperature which, in such circumstance, is that of the operating room.

By depressing the central nervous system, anesthetic agents depress the center of temperature regulation thus decreasing body temperature and contributing to the fall of temperature in the anesthetized patient. Sir George Pickering has emphasized this fact, by saying, "The best way to cool a patient is to anesthetize a patient."

Anesthetic agents cause cellular depression and decreases in metabolism and heat production. The effect of these agents on the "shivering center" and on the periphery in concert with muscle relaxants will block the act of shivering, and as long as the patient is anesthetized and paralyzed, no compensatory mechanism for heat gain exists. The fact that peripheral circulation has lost the capability of constriction will contribute further to the magnitude of heat loss in the anesthetized patient.

Premedication with any of the usual drugs has the effect of relaxing muscle tone, thus making the patient more susceptible to a fall in body temperature when taken into a cold operating room. On recovery from anesthesia, thermostatic reflexes appear, and if the body temperature is lowered, shivering and cutaneous vasoconstriction occur with a concomitant rise in oxygen consumption. The greater the fall in temperature, the greater the oxygen consumption during the recovery period.

In comparison with other anesthetic agents used, halothane can cause more heat loss during anesthesia, more shivering at the termination of anesthesia, and more rise in oxygen consumption.

The importance of increased postoperative oxygen consumption may be considerable, particularly in patients with preexisting respiratory or circulatory disease.

In the event that a postoperative airway obstruction exists, the patient will not be able to tolerate anoxia if, because of increased oxygen consumption due to shivering, the ventilation demand is increased. In patients with abdominal incisions and thoracotomy, increase in ventilatory demand may present postoperative difficulties.

Increase in oxygen requirement will also increase demands on circulation. Patients with cardiovascular problems and unreplaced blood loss will be further handicapped in dealing with this. During recovery from hypothermia, the rewarming acidosis can contribute greatly to morbidity of heat loss during anesthesia.

Robert M. Morris' study on the relationship between operating room temperature and the temperature of the anesthetized patient shows that a significant linear correlation exists between the patient's esophageal temperatures and their operating room temperatures. He classified the operating rooms according to their effect on patients' temperature: (1) rooms below 21°C in which all patients became hypothermic; (2) 21° to 24°C (70° to 75°F) rooms in which 70% of the patients remained normothermic and 30% became hypothermic; and (3) 24° to 26°C (75° to 79°F) rooms in which all patients remained normothermic. He concluded that, 21°C can be classified as the "critical ambient temperature" for lightly anesthetized paralyzed adults.

Boyan and his associates have shown that if, in addition, large amounts of cold blood are transfused, the fall in temperature can be greater. A contributing factor to this is the cold solution used for prepping. Deep anesthesia (with or without muscle relaxants) can also cause great heat loss. Since basal heat production decreases with age, the resultant heat deficit is greater in the elderly.

In addition to heat loss, secondary to vasodilation and decreased heat production, the opening of the abdominal cavity is an important factor with the anesthetized patient. Inside the peritoneal cavity is a large surface from which much heat can evaporate, and irrigation of the peritoneal cavity with cold solutions leads to increased heat loss. At a comfortable operating room temperature (20° to 22°C),

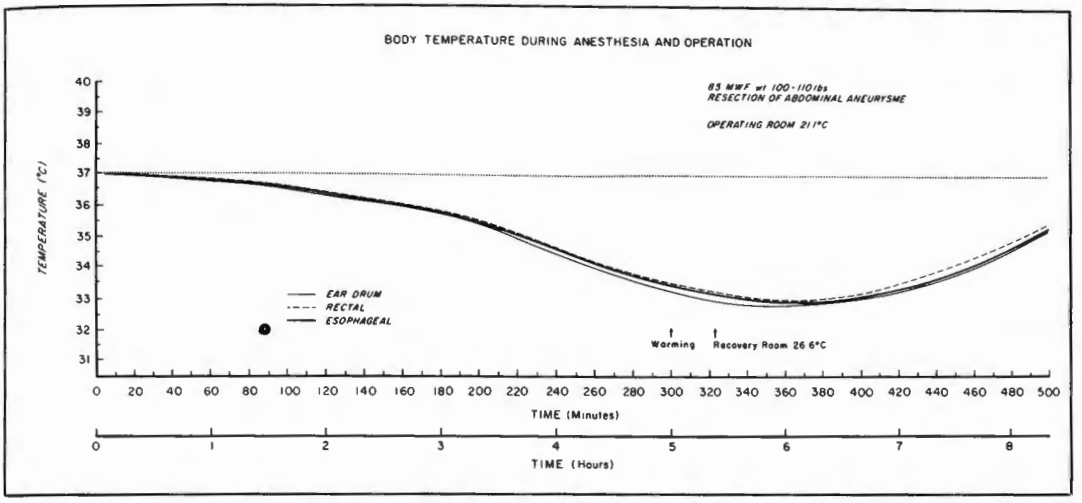

Fig. 8—Body temperature during anesthesia and operation. (Intra-abdominal)

most patients experience a fall in body temperature.

Figure 8 emphasizes the effects of age (85 years old), the type of operation (intra-abdominal), the length of procedure (5½ hours), and cold ambient temperature (operating room temperature 21.1°C) on the extent of the fall in body temperature. At times during the procedure, by means of a warm blanket, an effort was made to warm the patient. In spite of this effort, the drifting of hypothermia took place, and the patient regained a normal body temperature only after he was taken to the recovery room (temperature 26.6°C).

This is in concert with the observation of Robert M. Morris and his associates that a warm blanket under the paralyzed and anesthetized adult is no substitute for a warm operating room. One can see from this experiment that in the event of slow and progressive heat loss, there are minimal deviations in the monitoring of the different sites of body temperature. But under clinical circumstances when one can expect sudden heat gain and heat loss, we believe that it seems more important to use tympanic or esophageal monitoring of temperature.

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Nitrous Oxide-Curare Anesthesia: Reappraisal*

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Of the many inhalation drugs available today, nitrous oxide is the only one which is both non-explosive and non-toxic. Although the compound is rarely listed as a primary agent, it is used on almost every patient. The usefulness of nitrous oxide tends to be dismissed because it is considered to be relatively weak. However, with the continuing trend toward lighter anesthesia seen during the past quarter century, this viewpoint is no longer reasonable. The fact that MAC for halothane can be reduced to one third by the addition of 70% nitrous oxide attests to the drug's potency.

The experience of many practicing anesthetists throughout the United States indicates that anesthetic administration currently is more striking in its similarities than in its differences. It may even be said that a universal modern anesthetic sequence has evolved (fig. 1). First, almost everyone uses thiopental or some other barbiturate for induction, as a social necessity. Second, nitrous oxide in a concentration of 50% to 70% is invariably employed during the maintenance phase of anesthesia. Third, a muscle relaxant is used in most major cases, both to facilitate intubation and to produce surgical relaxation. Deep anesthesia is almost never relied upon. Finally, some other drug, perhaps halothane, ether, or Innovar may be adopted—in conjunction with nitrous oxide—for the maintenance of anesthesia. According to tradition this is called the primary agent. But with the aforementioned trend toward very light anesthesia, more often than not, this agent is adjunctive in nature. In fact, in some instances, an adjunctive drug is not used at all.

MODERN ANESTHETIC SEQUENCE

1. THIOPENTAL INDUCTION
2. NITROUS OXIDE
3. MUSCLE RELAXANT
4. (ADJUNCTIVE AGENT)

Fig. 1—Modern anesthetic sequence.

In the 1950's the British developed a technique in which very large doses of curare were used in combination with nothing more than nitrous oxide to produce the condition of anesthesia. No other adjunctive drug was used for maintenance. In this way, explosive agents were avoided. The process became known as the "Liverpool Technique" (Geddes and Gray, 1959). Part and parcel of the Liverpool Technique was the intentional production of respiratory alkalosis by hyperventilation. It was felt that alkalosis increased the depth of anesthesia. In recent years, however, the depressant effects of this condition have been questioned and, indeed, alkalosis itself has been shown to be not without its hazards.

During the past four years, we at Roosevelt Hospital have been increasingly interested in avoiding not only explosives but also potentially toxic agents. We have adopted essentially the Liverpool Technique (that is, nitrous oxide without supplementation, and curare) and modified it in two major aspects: we have employed normal ventilation, and we have modified the curare dosage. To date this technique has been applied to approximately 3,200 patients.

Technique. Figure 2 is a step-by-step description of the technique as we have employed it. Premedication has been variable, but we prefer a narcotic in the usual clinical doses. Thiopental is used for the induction of anesthesia in a dosage sufficient to abolish the lid reflex. One hundred percent oxygen is administered by mask for about two minutes, either prior to or immediately after the thiopental, and then after intravenous succinyl-

* Presented at the 25th Annual Stoneburner Lecture Series, February 26, 1972, at the Medical College of Virginia, Richmond.

1. PREMEDICATION: NARCOTIC PREFERRED
2. THIOPENTAL, 4-8 mg/kg
3. O_2 100% 2 MIN.
4. SUCCINYLCHOLINE 1 mg/kg
5. INTUBATION
6. N_2O 3.5 L, O_2 1.5 L.
7. VENTILATOR, MV = 90 ml/kg
8. CURARE: BY DOSAGE SCHEDULE
9. REVERSAL: NEOSTIGMINE 2.5 mg
   ATROPINE 1.0 mg
10. DECISION TO EXTUBATE

Fig. 2—Roosevelt Hospital's adaptation of the Liverpool Technique.

choline, endotracheal intubation is carried out. Immediately after intubation, nitrous oxide 3.5 liters and oxygen 1.5 liters are allowed to flow into the partial rebreathing circle system. This flow is then maintained throughout the remainder of the operation. A mechanical ventilator is employed in all instances promptly after intubation. The ventilator is set to deliver a calculated minute volume of 90 ml per kg. A relatively slow respiratory rate, approximately 8 to 10 per minute, with a relatively large tidal volume is preferred. The minute volume is routinely checked with a Wright ventilometer. With signs of returning muscle power following succinylcholine, curare is administered by a dosage schedule described in figure 5. Full curarization is maintained throughout the procedure. At the termination of the surgical procedure, reversal of curare is accomplished with the use of neostigmine 2.5 mg and atropine 1 mg given simultaneously intravenously and repeated once if necessary. Finally, a decision to extubate is made by clinical means. If the patient is capable of coughing vigorously on the endotracheal tube and of using his upper intercostal muscles to take a deep breath, and can lift his head off the table, the endotracheal tube is removed. If not, the patient is taken to the recovery room where mechanical ventilation is continued until full motor power returns spontaneously.

It should be noted that the above description of the nitrous oxide-curare technique contains nothing really extraordinary. Mechanical ventilation perhaps is not commonly employed, but it is generally accepted in modern anesthesia. Everything else on the list is very much a part of standard practice every day everywhere throughout the United States. Indeed, this sequence is really an example of the basic structure on which an anesthetic in this day and age is often built. What is surprising about the list, therefore, is not what is on it but what is missing from it. Note that there is no adjunctive drug listed. Or to use the more traditional terminology, there is no primary agent. Once the nitrous oxide is begun and the curare is given, no other agent is administered, either intravenously or by inhalation. Nitrous oxide is relied upon totally to produce unconsciousness, and curare is relied upon totally to keep the patient on the table.

Memory. The most significant question about this technique is whether 70% nitrous oxide by itself is enough to produce unconsciousness reliably in all patients. The only way to answer this is with the evidence of extensive experience. As mentioned earlier, we have used this technique fairly widely in all age groups on approximately 3,200 adult patients and in all types of surgery with the exception of intrathoracic procedures. Approximately two thirds of the cases were intra-abdominal. The technique has been used in operations ranging from one hour in length to well in excess of 6 hours, with an average of three hours, and it has been adopted for patients representing all grades of ASA physical status from 1 to 5, although the majority were either 2 or 3. As of this date, we know of no patient of the 3,200 who were actually receiving 70% nitrous oxide, who had any pain or any other conscious memory of the surgical procedure.

We did have five patients who remembered certain things due to a break in technique. Four of the five remembered either intubation or extubation. As a result, we have begun to use liberal amounts of induction thiopental and to continue nitrous oxide up to the moment of curare reversal. In one patient, a brief period of memory did occur during the operation. This patient remembered severe pain and a conversation which we knew did occur. On further investigation, however, we found that just before the period of memory the anesthetist had disconnected the endotracheal tube for suctioning for approximately 20 seconds. During this time the ventilator continued to operate. It emptied itself of nitrous oxide and drew air into the system through the open connector. For the next several minutes the patient received air instead of nitrous oxide.

We conclude that nitrous oxide in a concentration of 70%, does prevent memory totally and in all patients. However, the slightest break in technique

can result in memory and must be guarded against continuously.

Ventilation. A mechanical ventilator has been utilized in all cases in our experience. In addition, a Wright ventilometer is routinely used to verify the presence of proper minute volume. We have selected a figure of 90 ml per kg body weight for estimation of the minute volume on the basis of prior experience, both in the operating room and in our respiratory intensive care unit where arterial blood gas analysis revealed a $PaCO_2$ of between 35 and 45 mm Hg in most patients. This fact has also been documented in a study independent from ours (Ocbo and Terry, 1969).

Our real concern, however, was whether, with normocapnea, adequate arterial PO_2 levels could be reliably produced. We found in our early studies on healthy patients undergoing abdominal surgery, that PO_2's in excess of 100 mm Hg were produced routinely. However, in an attempt to look at the worst possible circumstance, we also studied 16 patients undergoing abdominal aortic graft procedures with 70% N_2O-curare anesthesia. Serial blood gas determinations during surgery yielded the results listed in figure 3. In no case was the PO_2 ever below 60

Abdominal Aortic Grafts
Mean Age 68 – 7 (S.D.)
ASA Status 2 – 4

Lowest PaO_2	Number
Under 60	0
60 – 69	4
70 – 79	6
80 – 89	1
90 – 99	3
100 +	2
Total	16

Fig. 3—Serial blood gas determinations during surgery with N_2O-curare anesthesia.

mm Hg, and in 12 of the 16, the lowest PO_2 recorded was above 70 mm Hg. While this does not indicate lush oxygenation, these PO_2 values probably do represent the normal levels for this age group. The average PCO_2 in this series was 38 mm Hg. It is worth repeating that a very slow ventilatory rate, 8 to 10 per minute with a relatively high tidal volume, was employed. It has been our experience that this ventilatory pattern yields consistently higher PO_2 values than a rapid, shallow pattern.

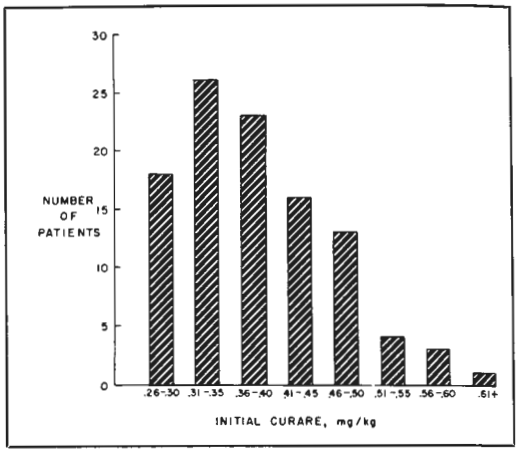

Fig. 4—Graph showing study of curare dosage necessary to produce paralysis.

We conclude that with normocapnea, adequate oxygenation can be produced, so long as the ventilatory pattern is proper, and so long as patients with severe intrapulmonary shunting, such as occurs in intrathoracic surgery, are avoided.

Curare Dosage. Traditionally, a clinically effective single dose of curare is said to be in the range of 0.5 to 0.6 mgm per kg body weight. In a series of 100 cases of patients undergoing elective surgery with thiopental-N_2O-O_2 anesthesia, we found that a dose of 0.3 mg per kg produced a clinically adequate degree of paralysis in about half the patients, as seen in figure 4.

From this experience we developed the curare dosage schedule outlined in figure 5. A dose of curare is calculated on the basis of 0.3 mg per kg and is administered to each patient. If this is not sufficient to

CURARE DOSAGE SCHEDULE

1. INITIAL
   a) 0.3 mg/kg
   b) IF INSUFFICIENT, 1 ml INCREMENTS
2. SUBSEQUENT DOSES
   a) GIVEN $\bar{q}$ 20–40 MIN
   b) EACH DOSE = $\frac{1}{2}$ PREVIOUS DOSE

Fig. 5—Outline of curare dosage schedule.

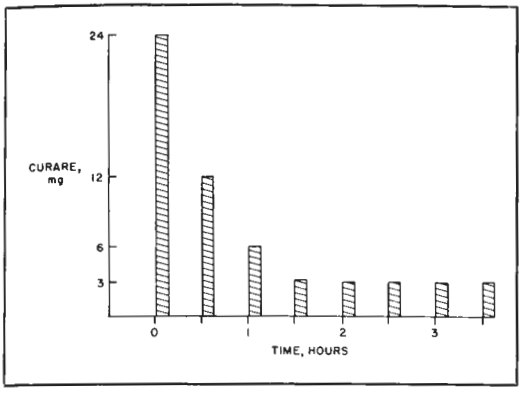

Fig. 6—Dosage schedule of curare administration.

abolish all coughing and respiratory activity, additional curare is administered in 1 ml (3 mgm) increments until all gross motor activity ceases. The total amount of curare is noted at this point, and becomes the basis for all subsequent doses. Each subsequent dose needs be only one half its previous dose, and it is required every 20 to 40 minutes when signs of returning muscle activity occur. When a dose of 3 mgm is reached, it is repeated, without halving, as necessary. An example of a dosage schedule in a typical case is shown in figure 6.

Using this dosage schedule, we have been able to reliably produce adequate continuous curarization with reasonable total curare doses. Figure 7 is a plot of the total curare dose in one hundred consecutive cases against the total duration of anesthesia. Total dose was clearly related to time. More important, the average dose was approximately 0.7 mg per kg which, for the average patient, represents a total of 50 mgm curare during a 3-hour anesthetic. This compares very favorably with the experience of the British.

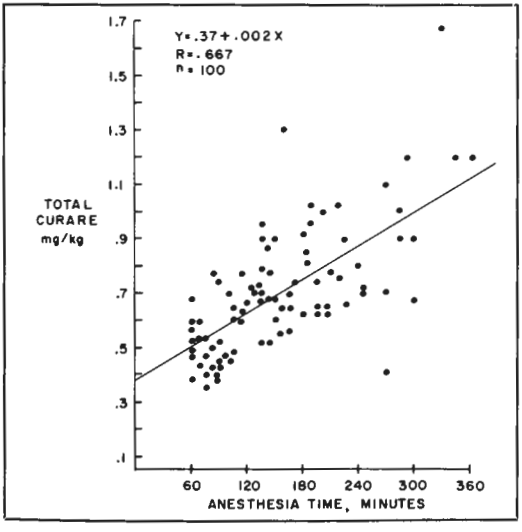

Fig. 7—Graph showing total curare dose as measured against duration of anesthesia in 100 cases.

Blood Pressure Changes. Significant hypotension incident to the administration of clinical doses of curare has been reported (Thomas, 1957). In our experience, however, this has not been a problem. Figure 8 is a compilation of the lowest and highest blood pressures noted in 100 patients, as measured by the cuff method, during the twenty minutes following the initial curare dose. While some patients responded with very low—and some with very high—blood pressures, the majority showed only mild changes, and no definite trend of clinical significance could be discerned.

Figure 9 is a plot of the degree of hypotension seen in those 55 patients in the series who suffered a fall in pressure, versus the dosage in each case. We could discern no dose-response relationship. We conclude that while curare has been reported by others to cause hypotension it does not do so to a clinically significant degree in the dosage range employed in this series.

Curare Reversal. Early in our experience we noted an occasional patient who was unable to maintain adequate spontaneous ventilation following the administration of neostigmine, even though these patients had not received excessive doses of curare. This was surprising in view of the well-documented fact that neostigmine is a highly predictable antagonist for curare (Bridenbaugh and Churchill-Davidson, 1968; Katz, 1967). However, review of these cases disclosed the fact that many had received intraperitoneal antibiotics of the type known to produce muscle paralysis (Pittinger, *et al.*, 1970), and all the others had been either hypothermic or hypovolemic at the time of attempted curare reversal. These factors have been shown to delay significantly the redistribution of curare (Dal Santo, 1964). Following this discovery we instituted the practice of omitting neostigmine reversal in those patients who had received intraperitoneal antibiotics, who were hypothermic, or in whom a hypoperfusion state was judged to be present. The endotracheal tube was left

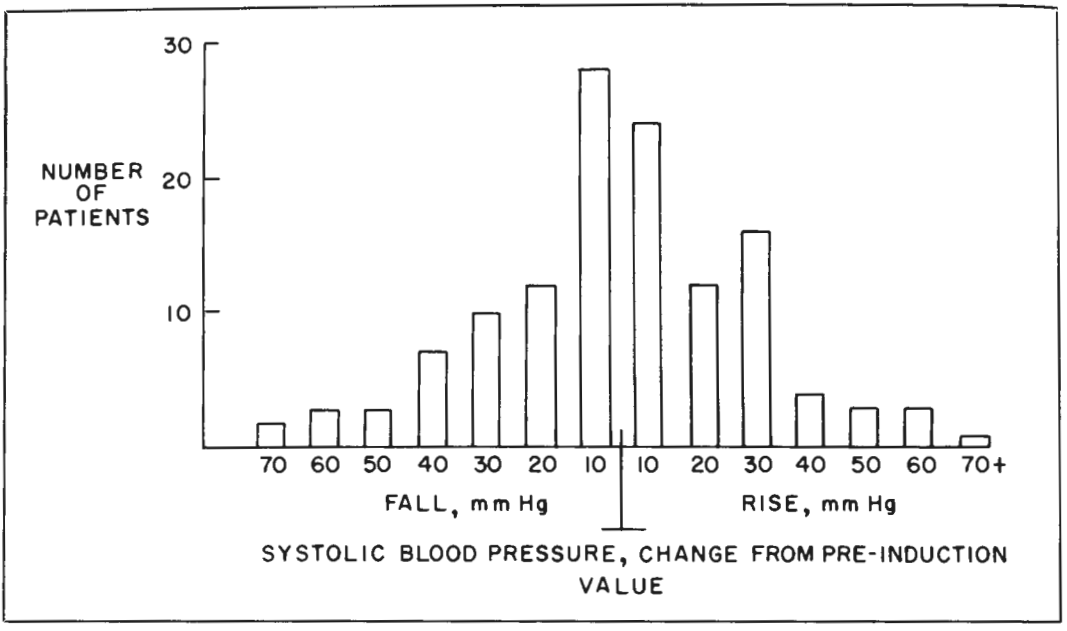

Fig. 8—Blood pressure readings of 100 patients following induction of curare.

in place, and muscle power was allowed to return spontaneously while the patient was ventilated mechanically in the recovery room. After the institution of this practice, experience in 100 consecutive patients was reviewed and is summarized in figure 10. Eighteen patients were intentionally not reversed; of these, six had undergone procedures, such as abdominal aortic grafts, in which postoperative mechanical ventilation is utilized in our institution as a matter of course. Hypoperfusion, hypothermia, the use of intraperitoneal antibiotics, or a combination of these, were present in all other instances.

Of the 82 cases in which neostigmine was employed, only one failed to develop adequate spontaneous ventilation, and in this one case, severe hypovolemia from unrecognized surgical blood loss was noted shortly thereafter; spontaneous ventilation returned with the transfusion of two units of whole blood. We conclude that neostigmine is indeed a predictable antagonist for curare so long as the pathologic conditions noted above are excluded.

Conclusions.

1. Seventy percent N_2O, as a sole depressant agent, is adequate to prevent pain and memory in 100% of cases. There is no evidence

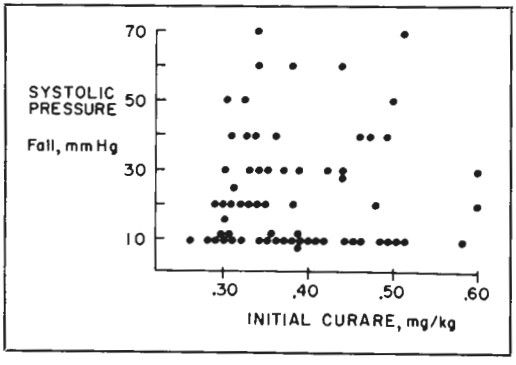

Fig. 9—Graph showing degrees of hypotension in patients as measured against individual curare dosage.

CURARE NOT REVERSED: 18 PATIENTS	
1. PLANNED POSTOP. VENTILATION	6
2. HYPOPERFUSION	7
3. HYPOTHERMIA	6
4. I. P. ANTIBIOTIC	7

Fig. 10—Results of review where curare was not reversed.

that it is ever inadequate as an anesthetic, even in deep intra-abdominal operations. Therefore, with this technique, the use of other potent depressant agents either by inhalation or by vein is unnecessary. Major organ toxicity is thus avoided, and recovery from anesthesia is prompt. Furthermore, major cardiovascular abnormalities occurring during surgery can be assumed to be due to factors other than anesthesia, since neither N_2O nor curare alter cardiovascular function significantly.

2. Curare dosage need not be excessive. When used according to the recommended schedule, it is well within the range known to be successfully antagonized with neostigmine and below the level known to produce significant hypotension.
3. Hypoxia need not occur, so long as mechanical ventilation is properly applied and meticulously measured. Whenever there is doubt, arterial blood gas analysis should be available.
4. Curare reversal has proved to be successful in all cases except in those instances in which there is some pathologic process which delays curare redistribution such as hypovolemia, or hypothermia, or in those instances in which intraperitoneal antibiotics are used. In those cases, one must be prepared to utilize postoperative mechanical ventilation.

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Myocardial Infarction After General Anesthesia*

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A survey by the National Center for Health Statistics estimated that there were 111.1 million adults in the United States between 18 and 79 years of age during the years 1960 to 1962. Of these, 3.1 million had definite, and 2.4 million had suspected, coronary heart disease. Definite myocardial infarction had occurred in an estimated 1.4 million adults (USNCHS, 1965). The number of patients with coronary heart disease, or myocardial infarction, who require some form of surgical operation will increase steadily as the population increases. Considering the stress of anesthesia and surgery, these patients present problems related to their specific cardiac pathology.

In spite of these large numbers, few statistics are available about the incidence of primary or recurrent myocardial infarction after anesthesia. Mortality rates and their relation to age and sex, and to type and duration of anesthesia in existing reports, are based on a relatively small number of cases. This review attempts to provide additional data on these questions by analyzing a 2-year experience in a large anesthetic practice.

Material and Method. During the years of 1967 and 1968, 32,877 patients 30 years of age and over underwent some form of operation or diagnostic procedure under general anesthesia at our institution. Cardiac operations were not included. Among these, 422 patients had evidence of previous myocardial infarction by history or by electrocardiography before operation. Their distribution for these years is shown in Table 1. Twenty-eight of them (6.6%) reinfarcted after operation during the first week, as indicated by clinical symptoms, electrocardiogram (ECG), enzyme studies, or postmortem examination. Forty-three other patients also had infarctions during this same postoperative period—0.13% of all patients without previous history of myocardial infarction, having anesthesia (Table 1).

The relationship of patients with previous myocardial infarction to surgical population by age and sex, and their reinfarction ratio, is shown in Table 2. Myocardial infarction is primarily a disease of men. Of every 1,000 anesthetized, 12.8 patients had had a previous myocardial infarction. Fifteen of 28 patients died after reinfarction (54%), with 12 of these deaths occurring during the first 48 hours after myocardial infarction (80%) (Table 3). Forty-three of the 71 patients who infarcted had no previous evidence of myocardial infarction, but 16 had known coronary heart disease with angina. The other 27 had no history of coronary disease, but 6 of them were

TABLE 1. Incidence of myocardial infarction related to previous infarction.

History	General anesthesia (no.)	Myocardial infarction 1st wk postop	
		No.	%
Previous myocardial infarction			
1967	218	13	6.0
1968	204	15	7.4
Total	422	28	6.6
No previous myocardial infarction			
1967	15,597	19	0.12
1968	16,858	24	0.14
Total	32,455	43	0.13

* Delivered by Emerson A. Moffitt, M.D. at the 25th Annual Stoneburner Lecture Series, Feburary 26, 1972, at the Medical College of Virginia, Richmond. Reprinted with permission from the *Journal of the American Medical Association*, 220:1451–1454, 1972.

TABLE 2. Relation of myocardial infarction to previous infarction and to surgical population.

Age	General anesthesia (no.)	Total previous myocardial infarction/1,000 anesthetics	Myocardial infarction in men		Myocardial infarction in women	
			Previously	Again postop	Previously	Again postop
30 to 39	4,081	0.7	3			
40 to 49	6,906	3.6	24	2	1	
50 to 59	8,825	10.5	75	5	18	
60 to 69	8,375	20.9	147	13	28	
70 to 79	4,051	27.9	90	6	23	1
80+	639	20.3	10	1	3	
Total	32,877	12.8	349	27	73	1

diabetic and 10 had hypertension requiring treatment. The mortality rate of these first infarctions is also high.

The patients received a variety of general anesthetic agents and muscle relaxants (Table 4) without influencing the incidence of reinfarction. Duration of anesthesia ranged from 20 minutes to 6 hours, yet the incidence of reinfarction did not change as time increased (Table 5).

The relationship of site and type of operation to recurrence of myocardial infarction is shown in Table 6. When analyzed by the chi-square test, the reinfarction ratio in operations of the thorax and upper abdomen was significantly higher ($P < 0.001$) than for other types of operation (Table 6).

The relationship of incidence of postoperative infarction to interval since previous myocardial infarction is shown in Table 7. Thirty-seven percent of patients operated on within 3 months of myocardial infarction had postoperative reinfarctions. This decreased to 16% in patients between 3 and 6 months after infarction, and remained 4 to 5% in patients more than 6 months after previous infarction.

The figure depicts the distribution of myocardial infarction on various postoperative days. There were significant day-to-day differences in the frequency of myocardial infarction, the third day being highest ($P < 0.01$).

Six of the 28 patients did not have chest pain with reinfarction. Suspicion of an acute infarct came from the postoperative ECG, or from clinical findings such as irregular pulse, leading to a full investigation.

Discussion. Coronary heart disease may begin early in adult life, but rarely manifests itself before 45 years of age. Myocardial infarction is much more common in men than women, and its prevalence rises with age, the 65 to 74-year-age group having the greatest incidence. This was also true in the surgical population, yet the reinfarction ratio did not change significantly in our study for older age groups. Our present study also indicates that patients with previous myocardial infarction who have

TABLE 3. Preoperative heart disease and myocardial infarction after general anesthesia.

Preoperative status	Cases	Myocardial infarction in first wk postop			
		Deaths			
		Total		In 48-hr-postoperative myocardial infarction	
		No.	%	No.	%
Myocardial infarction	28	15	54	12	80
Coronary heart disease					
Known	16	14	87	9	64
Unknown	27	15	56	11	73
Total	71	44	62	32	73

general anesthesia and surgery have a 50-times greater chance of reinfarction than those who do not have a history of myocardial infarction.

Reports on rates of postoperative myocardial infarction differ widely. Baer, *et al* (Baer, *et al.*, 1965) report that 41 of 150 patients older than 30 years of age had myocardial infarction after operation. Walker and Macdessi (Walker and Macdessi, 1966) found evidence of myocardial infarction among 26 of 100 patients older than 65 years. Patients in both these studies were randomly selected and some had previous myocardial infarction or evidence of coronary heart disease. Knapp, *et al* (Knapp, *et al.*, 1962) reported that among 427 patients with a previous history of coronary occlusion, 26 had reinfarctions. Arkins, *et al* (Arkins, *et al.*, 1964) collected a series of 240 patients with previous myocardial infarction, of whom 54 died during the first 2 months postoperatively. Mauney *et al* (Mauney, *et al.*, 1970) relates a prospective study in which 30 of 365 patients, age 50 years or over, had myocardial infarction after operation, with 16 deaths.

Comparing these figures is difficult because of the wide variety of factors involved such as age, type of hospital, methods of diagnosing myocardial infarction, other preexisting illnesses, kind of operation, and postoperative care. However, one conclusion is common to all reports: the high incidence of postoperative myocardial infarction in patients who had had previous infarction, even when the infarction was long before operation.

Fifty-four percent of our patients who had previous myocardial infarction died as a result of recurrent myocardial infarction (similar to the 53% mortality cited by Mauney, *et al* [Mauney, *et al.*, 1970]). By comparison the mortality rate from myocardial infarction in a general hospital is approximately 30% and in a coronary care unit this may be reduced to 15 to 20% (Logue and Hurst, 1970). So myocardial infarction, or recurrent infarction, after anesthesia and a major operation, is more serious and lethal than myocardial infarction alone.

TABLE 4. Relation of myocardial infarction to anesthetic agents.

Agents and mixtures	Myocardial infarction		
	Previously	Again postop	% again
Thiopental, O_2, N_2O, tubocurarine			
With methoxyflurane	57	5	8.8
With halothane	268	18	6.7
With ether	66	4	6.1
With pentazocine	3		
Thiopental, O_2, N_2O	21		
With halothane, gallamine	1	1	...
With gallamine	1		
With cyclopropane	1		
Thiopental, diazepam	2		
Thiopental, O_2, surgical infiltrate	1		
Innovar, O_2, N_2O, tubocurarine	1		
Total	422	28	6.6

Others have reported that the shorter the interval from previous myocardial infarction to major operation, the greater the hazard of reinfarction (Knapp, *et al.*, 1962). In the series of Arkins *et al* (Arkins, *et al.*, 1964), 27 patients had infarction under 3 months old; 11 of them (40%) died during or after operation. In 10 of these patients the cause of death was directly related to myocardial infarction. In our series the reinfarction rate was 37% among the patients with infarction less than 3 months previously; the incidence dropped to 16% when the myocardial infarction was 3 to 6 months old. Because the reinfarction rate was stable at 5% after 6

TABLE 5. Duration of anesthesia and myocardial infarction after general anesthesia.

Anesthesia, min	Myocardial infarction in men		Myocardial infarction in women		Myocardial infarction again (%) (M + W)
	Previously	Again postop	Previously	Again postop	
0 to 59	35	3	11		6.5
60 to 119	66	4	12		5.1
120 to 179	39	4	14		7.5
180 to 239	20	1	4		4.2
240 to 299	12		3	1	6.7
300 to 359	2				
Total	174	12	44	1	6.0

TABLE 6. Relation of myocardial infarction to site and type of operation.

Site and type of operation	Myocardial infarction in men		Myocardial infarction in women		Myocardial infarction again (%) (M + W)
	Previously	Again postop	Previously	Again postop	
Thorax & upper abdomen	(113)	(15)	(18)	(1)	(12.2)*
Great vessels	49	5	5		9
Lung	14	5			36
Other intrathoracic	4	3			75
Biliary, upper abdomen	46	2	13	1	5
Other	(236)	(12)	(55)		(4.1)*
Extraperitoneal abdominal	5	1	2		14
Endoscopic: oral	8	2			25
perineal	5	2			40
Perineal GU	48	2			4
Anorectal	7	1			14
Vertebral column	14	1	2		6
Extremities, bone	18	2	5		9
Head and neck	13	1	5		6
Miscellaneous	118		41		
Total	349	27	73	1	6.6

* Difference between groups is significant ($P < 0.001$).

months, elective surgery should be postponed beyond this time. Only life-threatening emergencies should be considered for surgery less than 6 months after a myocardial infarction.

About one third of patients having myocardial infarction alone die in the first 48 hours (Shapiro, *et al.*, 1969). However, 80% of our postoperative patients died within 48 hours after myocardial infarction, which suggests that arrhythmia, rather than a low cardiac output due to myocardial failure, may be the primary cause of death. Since these infarcts occurred in hospitals, one can reasonably assume that a lower mortality rate could be obtained if all those patients with previous coronary heart disease and myocardial infarction were monitored carefully and early measures taken to treat rate and rhythm disturbances. Intensive monitoring and care are needed.

Several factors may precipitate myocardial infarction during and after operation, such as tachycardia, hypoxemia, hypotension, hemorrhage, and lowered cardiac output (Dack, 1963). These complications are more frequent after surgery of the great vessels, lung, and the upper abdomen. As a group, these more major kinds of operation were followed by three times more infarctions than any other type of operation. This fact indicates the need

TABLE 7. Relation of myocardial infarction to interval from previous myocardial infarction.

Months	Myocardial infarction in men		Myocardial infarction in women		Myocardial infarction again (%) (M + W)
	Previously	Again postop	Previously	Again postop	
0 to 3	8	3			37
4 to 6	15	3	4		16
7 to 12	31	2	11		5
13 to 18	26	1	1		4
19 to 24	19	1	2		5
25+	186	10	46	1	5
Old myocardial infarction, age not recorded	64	7	9		10
Total	349	27	73	1	6.6

for close attention to maintaining optimal blood volume and pressure in the postoperative period.

Six of 28 of our patients had silent recurrent infarction discovered electrocardiographically or clinically after operation. Chest pain at this time may be absent or obscured because of narcotics and sedatives. Serial electrocardiographic tracings daily for up to a week after operation, for comparison with a baseline ECG taken prior to operation, are indicated in patients who have hypertension, coronary disease, and previous infarction.

Hypoxemia when breathing air occurs to some degree after most general anesthetics and major operations. We have found in a different study that after abdominal surgery arterial oxygen tension decreases for at least 3 postoperative days (2%, 11% and 12% respectively), largely due to miliary atelectasis, pulmonary shunting, and possibly decreased cardiac output (Tarhan, *et al.*, 1969). Another reason, then, for having patients who have had previous infarction, and those who have coronary disease, in intensive care areas postoperatively is that they can be oxygenated better. They need not only an increased inspired oxygen tension for several days but also special attention to chest physiotherapy—coughing, deep breathing, chest pounding, regular turning, and dangling of the legs. By these means, atelectasis may be minimized, myocardial oxygen supply kept adequate, and infarction avoided.

That there is a tendency for excessive thrombus formation in men who have had previous myocardial infarction has been suggested (Goldenfarb, *et al.*, 1971). The coagulability of blood is increased during the second to seventh postoperative days (Grigoryan and Alimov, 1969). Results of prolonged anticoagulation to prevent recurrent myocardial infarction have been controversial in the past (Seaman, *et al.*, 1964), yet short-term (up to 1 week) prophylactic anticoagulation for postoperative recurrent myocardial infarction has not been tried to our knowledge.

The significance of the combined effects of all these factors on the incidence of myocardial infarction after operation, especially during the third postoperative day (fig. 1), is not clearly documented. Certainly these high-risk patients should be watched closely and treated agressively, postoperatively, in an attempt to make anesthesia and surgery safer for them.

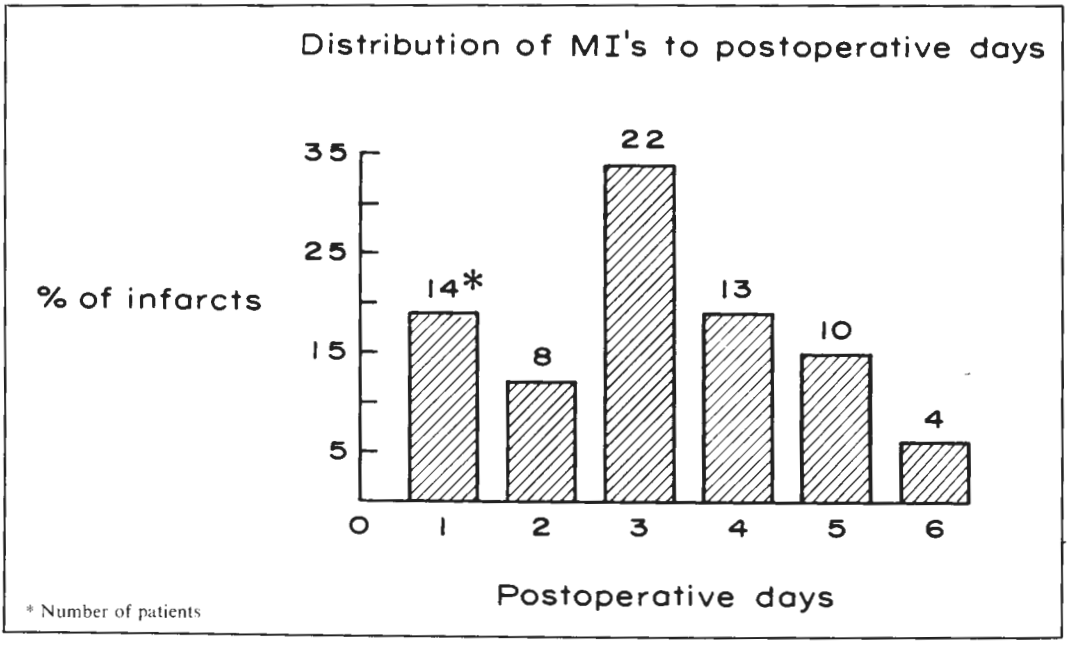

Fig. 1—Distribution of myocardial infarctions to postoperative days.

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Progress of Congenital Heart Disease: The Team Approach as It Includes the Anesthesiologist*

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Historical Background. No branch of medicine has progressed more rapidly and dramatically in the last 35 years than Pediatric Cardiology. Harvey's description of the circulation in 1628 (Harvey, 1628) and Leonardus Botallus' (Noback and Rehman, 1941) report on the fetal circulation were milestones in clarifying our understanding. Isolated clinical and pathologic descriptions of specific lesions written with amazing accuracy appeared in the 17th and 18th centuries. Sandifort (Sandifort, 1777) in 1777 presented details of a clinical examination correlated with necropsy findings in a cyanotic 12-year-old boy with pulmonic stenosis and a ventricular septal defect long before Dr. Fallot's famous report (Fallot, 1888). Chauveau and Marey (Chauveau and Marey, 1863) performed a right heart catheterization in 1861, but the technique was forgotten until Walter Forssman (Forssman, 1929), a urologist, reviewed it in 1929. Forssman even attempted an angiocardiogram, but the contrast injected was too dilute to be visualized and he was told by his associates that his work qualified "for a circus not a clinic." Despite such criticism, with Cournand and Richards, Forssman received the Nobel Prize in 1956.

The modern era of Pediatric Cardiology began with Dr. Maude Abbott, whose meticulous Atlas, published in 1936, presented precise descriptions of 1000 cases of congenital heart disease which she had personally examined from a pathologic standpoint (Abbott, 1936). She added a review of the development and comparative anatomy of reptilian, amphibian, and mammalian hearts. After reviewing the world literature related to the pathology of congenital cardiac malformations, she added her cases and published many comprehensive reports of individual lesions. As a result of her work, a few clinicians began to diagnose specific congenital heart lesions, although usually therapy was hopeless. Suddenly in 1938, the modern era of cardiac surgery began when Dr. Gross first successfully ligated a patent ductus arteriosus (Gross and Hubbard, 1939). Munro of Boston had suggested ligating a patent ductus as early as 1907 (Munro, 1907), but it was 30 years later before Strieder (Graybiel, *et al.*, 1938) attempted the technique. While Crafoord (Crafoord, 1965) in Sweden was ligating a patent ductus, the suture severed the vessel. It was necessary to clamp the aorta for 28 minutes. To his surprise, the patient did well and he recognized that this occlusion could be tolerated both by the heart and nervous system. Soon thereafter, in 1944, he successfully repaired a coarctation of the aorta in an 11-year-old boy (Crafoord and Nylin, 1945).

Successful surgery was a great stimulus to the diagnosis of acyanotic congential heart disease. About this time, Dr. Park, Professor of Pediatrics at Johns Hopkins, assigned Dr. Helen Taussig to the cardiology clinic suggesting that she accumulate data and correlate clinical information and pathologic findings on children with congenital heart disease. She quickly noted the repetitive patterns of developmental malformations and learned to make amazingly accurate diagnoses. Her monograph, published in 1947, was the first textbook on congenital heart disease (Taussig, 1947). Dr. Alfred Blalock recalled a small conference where he was discussing experimental production of pulmonary hypertension in animals using a systemic artery to pulmonary artery anastomosis. Dr. Taussig asked if he could increase the pulmonary blood flow in patients with pulmonic stenosis in the same way (Blalock, 1966).

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* Presented at the 25th Annual Stoneburner Lecture Series, February 26, 1972, at the Medical College of Virginia, Richmond. Portions of this study are reprinted with permission from the *Virginia Medical Monthly* 98:408, August 1971.

She was thinking of the many cyanotic children with decreased pulmonary blood flow as observed in tetralogy of Fallot or pulmonary atresia. No one knew the answer to three major questions: (1) Could a blue child tolerate anesthesia? (2) Could one occlude a pulmonary artery temporarily, especially in a blue child? (3) Would the arm tolerate ligation of the subclavian artery? Many animal experiments were carried out to attempt to answer these questions before they recognized that the answer to each was yes. The first Blalock-Taussig shunt for a tetralogy of Fallot was created successfully in 1944 (Blalock and Taussig, 1945). Modifications of the shunt procedure (Potts, *et al.*, 1946; Waterston, 1962) and Sir Russell Brock's (Brock, 1948) alleviation of valvular pulmonic stenosis followed quickly. Scott (Scott, 1955) at Vanderbilt in 1954 achieved open correction of a tetralogy with hypothermia, but it remained for Lillehei (Lillehei, Cohen, *et al.*, 1955) and Varco in Minneapolis, utilizing cross circulation, to first close a ventricular septal defect and completely remove right ventricular obstruction in 1955.

Gibbon had been working on a heart lung machine since the early 1930's and performed the first successful operation closing an atrial septal defect by this method in May, 1953 (Gibbon, 1954) Crafoord visited Gibbon in the late 1930's and his group simultaneously worked on a heart lung machine and developed a disc oxygenator. The advent of open heart surgery made possible accurate correction of the many complex congenital heart defects. Dr. Crafoord (Crafoord, 1965) considers the development of the Engstrom-Bjork respirator for anesthesia and postoperative ventilation a milestone in operative and postoperative care.

Developments in the physiology laboratory, including refinements in the technique of cardiac catheterization and particularly the addition of angiocardiography, as introduced by Robb and Steinberg (Robb and Steinberg, 1938), made precision in diagnosis possible. Improvements in the toxicity of contrast media made cineangiography less dangerous for small infants. Improved electronic equipment for recording and monitoring pressures and utilization of colorometric methods for rapid determination of oxygen saturations and indicator dilution increased the safety and efficiency of diagnostic cardiac catheterization. Rapid measurement of blood gases and electrolytes added another safety feature.

Transposition of the great arteries was first palliated in infancy in 1940 by Blalock and Hanlon (Hanlon and Blalock, 1948), by creating an atrial septal defect. This gave only temporary and moderate relief, but the frequency of this defect and its lethal characteristics were a continuing challenge to devise corrective surgery. Baffes (Baffes, 1956) attempted to reverse venous return. Senning (Senning, 1959) reported the first correction by plastic revision of the atria to reverse venous inflow in 1959. Mustard's (Mustard, 1964) use of an intra-atrial pericardial patch for total correction has vastly improved the prognosis in this previously hopeless lesion. In 1966, Rashkind and Miller (Rashkind and Miller, 1966) described the catheterization balloon technique for creating a large atrial septal defect, permitting survival through the critical neonatal period.

The achievement of success in correcting a complete truncus arteriosus or a complete atrio-ventricular canal captured the imagination of Rastelli and, based on a vast knowledge of anatomy, embryology, and physiology, has been achieved (Rastelli, Weidman, and Kirkland, 1965; Rastelli, Titus, and McGoon, 1967). The eight major congenital heart lesions now have excellent corrective procedures with acceptable mortality rates, which have diminished as preoperative diagnosis, surgical skill, and postoperative intensive care have improved. Rarer lesions are more hazardous and difficult to correct, especially in the younger child. The neonate, whose complex varieties of heart disease lead to cardiac failure and cyanosis early, needs early, aggressive diagnosis to avoid a 75% mortality. With ideal treatment, about ½ of the deaths can be prevented.

Auxillary aids in the care of a child with congenital heart disease lie in the fields of anesthesiology, hematology, biochemistry, and electronics. Landsteiner's (Landsteiner, 1901) description of blood groupings was essential for transfusions. A purified heparin, which allowed standardization and control of coagulation of blood, was a prerequisite to modern cardiac surgery. Pacemakers, defibrillators, prosthetic valves, and patches, now used routinely, have all been developed in the last few years.

The Medical College of Virginia assumed a position of leadership in modern aspects of cardiovascular and thoracic surgery under the direction of Dr. I. A. Bigger. There have been times, especially as open heart surgery began in the 1950's when this was a difficult role to maintain. The success of the

surgical effort is dramatically illustrated by the analysis of mortality statistics from the University of Minnesota for all open heart procedures on patients with congenital heart disease (Lillehei, Varco, *et al.*, 1967)

Progress of Open Heart Surgery for Congenital Heart Disease University of Minnesota

	Number of Cases	Operative Mortality
1954–1957	386	36%
1958–1962	986	22%
1963–1966	419	12%

At the Medical College of Virginia, my colleagues[1] have participated with me in a recent study to determine the incidence, morbidity, and mortality of surgically corrected congenital heart lesions over a six-year period. Our findings are stated below.

Materials and Methods. All patients, private or staff, who had surgery for correction or palliation of a congenital cardiac defect from birth to 20 years of age at the Medical College of Virginia Hospitals between January 1, 1966 and January 1, 1972 are included in this report. This six-year interval presents a complete evaluation of our recent surgical results. Every patient had a complete cardiac evaluation, including a history, physical examination, chest roentgenogram and electrocardiogram. Cardiac catheterization and angiocardiography were done except in children with a patent ductus arteriosus in whom these diagnostic procedures were frequently omitted. Decisions for surgery were made at a weekly conference in which the pediatric cardiologists, physiologists, radiologists, pathologists, and surgeons participated. Surgical procedures were divided approximately equally between the two surgical teams. During these six years, there were:

11,831	pediatric cardiology out-patient visits
2,985	hospital patients
557	children undergoing surgery for congenital cardiac defects
593	total surgical procedures for congenital cardiac lesions
45	deaths

[1] Dr. H. Page Mauck, Jr., Dr. Jon B. Tingelstad, Dr. Louise W. Robertson, and our surgeons, Dr. Richard R. Lower and Dr. Lewis H. Bosher, Jr.

Results. Five hundred fifty-seven children had major surgical procedures with the distribution as shown in Table I. The mortality for the common defects will be considered individually. Any death within the first month postoperatively is considered as surgical mortality. For the 593 procedures, there was a 7.58% mortality.

Atrial Septal Defects. Even a small atrial septal defect makes a preschool child a candidate for surgery. This was the most frequently corrected left to right shunt and was seen in 98 patients divided into the following types:

Secundum	72
Primum	15
With Partial Anomalous Pulmonary Venous Return	9
Single Atrium	2

All were catheterized and patients with a pulmonic to systemic flow ratio greater than 1.4:1 were referred for surgery at an appropriate age. The span was 11 months to 20 years. One infant with heart failure was corrected at 11 months. The mean age for correction was 6 years. There were no deaths in this group.

Ventricular Septal Defects. Eighty patients had closure of a moderately large ventricular septal defect which was the major lesion. The types are as noted (Table II) and include two with more than one defect and five with a LV-RA shunt. There were many associated defects, including atrial septal defects, aortic insufficiency, and patent ducti. Seven infants with intractable cardiac failure had pulmonary artery banding to decrease pulmonary blood flow caused by a large left to right shunt through the defect. Seven children required removal of a previously placed pulmonary artery band, in addition to closure of the defect. Two children have been reoperated for closure of a residual shunt. Severe aortic insufficiency from a redundant aortic cusp led to one surgical death. Of the seven infants under one year of age who required pulmonary artery banding, only four have good surgical palliation. Associated intra and extra cardiac defects complicated their course.

Patent Ductus Arteriosus. A patent ductus arteriosus has been interrupted in 90 patients between the ages of 3 months and 19 years. Almost all have been seen postoperatively and discharged as

TABLE I
INCIDENCE CONGENITAL DEFECTS

Defect		Patients (557 Patients) (593 Procedures)	Expired (45)	MCV Mortality % (8.07%) (7.58)
Acyanotic				
Atrial Septal Defect		98	0	0
Ventricular Septal Defect		87	4	4.6
Patent Ductus Arteriosus		90	2	2.2
Coarctation		34	1	2.9
Pulmonic Stenosis		36	0	0
Aortic Stenosis		15	0	0
Vascular Rings		5	1	20
Miscellaneous Acyanotic		3	0	
Cyanotic				
Tetralogy of Fallot		118		
Shunts	61		8	13.1
Open Correction	63		3	4.7
Thoracotomy	1		0	0
Pacemaker	1		0	0
Transposition of Great Vessels		21		14.2
Palliative	17		3	17.6%
Mustard Procedure	4		0	0
Rare Cyanotic Lesions		50	23	46

cured. Two children, one an infant, died of technical problems during surgery. Because of cardiac failure and marked cardiomegaly, eleven infants were surgically corrected under one year of age. Ideally, surgery is deferred until the child is greater than 2 years of age. Several premature infants on whom the diagnosis was confirmed had spontaneous closure of their ductus.

Coarctation of the Aorta. Coarctation of the aorta was corrected in 34 patients at a mean age of 6 years. All patients had preoperative aortography. Four patients required surgery in infancy for intractable congestive failure, of whom one infant died. Successful correction of a complete interruption of the aortic arch has been done on two occasions.

TABLE II
VENTRICULAR SEPTAL DEFECTS (87)

Types:			
Corrected		80	
Single	73		
(Removal of Bands 7)			
Multiple	2		
LV-RA Shunts	5		
Banded Pulmonary Artery		7	
Ages:			6 Weeks–20 Years
Deaths:			4 (4.6%)
Correction	2	(2.5%)	
Pulmonary Artery Bands	2	(28.5%)	

Pulmonic Stenosis. Pulmonic stenosis is commonly associated with other defects, but was seen as the primary problem in 36 children who had an intact ventricular septum and a right ventricular to pulmonary artery systolic gradient between 50 and 160 mm. Hg. The age span was 11 days to 18 years and two infants were less than 1 year of age. The types are as follows:

Valvular	28
Supravalvular	1
Primary Infundibular	4
Rubella with Valvular Pulmonic Stenosis and Peripheral Pulmonic Stenosis and Patent Ductus Arteriosus	3

Associated defects included atrial septal defect and peripheral pulmonic stenosis in five. An associated rubella syndrome with a patent ductus occurred in three babies. Secondary infundibular obstruction required surgical alleviation in about ½ of the valvular cases. All survived and were improved.

Aortic Stenosis. Although 80 cases of aortic

stenosis were studied in the cardiac catheterization laboratory in this six-year period, only 15 were referred for surgery. The age span was 3 years to 19 years. The types were as follows:

Valvular	10
Subvalvular Membrane	2
Idiopathic Hypertrophic Subaortic Stenosis	1
Supravalvular	1
With Severe Aortic Insufficiency	1

Criteria for operation were a gradient in excess of 60 mm Hg and electrocardiographic evidence of left ventricular hypertrophy and strain. This age group is older than for most other lesions and included no infants. Those with valvular stenosis underwent valvuloplasty; only one prosthetic valve was utilized in a 15-year-old girl with severe aortic insufficiency. A teflon patch was employed to widen the boy's supravalvular aortic stenosis. Four patients with aortic insufficiency initially continued to manifest mild valvular incompetence.

Vascular Rings. Five patients with an aortic vascular ring were repaired under 8 months of age. One infant with a left pulmonary artery arising from the right pulmonary artery causing a vascular sling did not survive the surgical procedure. All others had relief of their stridor and have improved after 1 to 5 years. One infant also had a shunt for severe tetralogy.

Miscellaneous Acyanotic Lesions. An anomalous right coronary artery arising from the pulmonary artery was repaired successfully by direct anastomosis to the aorta in a 12-year-old boy. An arterio venous fistula between the external carotid artery and the internal jugular vein was also repaired last year.

Tetralogy of Fallot. One hundred eighteen children had 126 primary surgical procedures for tetralogy of Fallot (Table III). In general, a Waterston's shunt (aorta to right pulmonary artery anastomosis) was the procedure of choice in the first three months of life, a Blalock-Taussig shunt (subclavian to pulmonary artery) being preferable if one was required in a slightly larger child. Thirty-six infants had shunts created within the first year of life, of whom twenty eight survived. In 1970, six infants with a complete pulmonary atresia with a ventricular septal defect had emergency surgery attempted in the first few weeks of life; only two survived. There were no deaths in children who had shunt procedures over 1 year of age. The mortality for the shunt, including those with pulmonary atresia, is 13.1%. Seven patients required revision of their shunt at some time postoperatively. The majority were treated with digitalis in the postoperative period, since cardiac failure was a frequent transient complication.

TABLE III
TETRALOGY OF FALLOT
(126) Primary Procedures
(118) Children

Types:			
Shunts			61
Open Correction			63
Previous Shunts		28	
No Previous Shunts		35	
Thoracotomy			1
Pacemaker			1
Secondary Procedures			11
Revision of Shunts	7		
Secondary Repairs	4		
Deaths:			
Mortality Shunts			8 (13.1%)
Mortality Correction			3 (4.7%)
Total			11 (8.8%)

Open correction of tetralogy in 63 patients was successful in 60, giving this a mortality of 4.7%. This surgical procedure is generally reserved for those over 40 pounds with an age distribution as noted in fig. 1. The youngest child was 3 years old and weighed 27 pounds. Of the 63 children undergoing open correction, 35 had no previous shunt. Twenty-eight had shunting surgery in the past and 8 had both procedures during the six years of study. Transient cardiac failure postoperatively occurs frequently, but responds well to digitalis and diuretics. Permanent complete heart block occurred in 2 children; one died suddenly soon after the operation; the other now has a pacemaker implanted. Four children have required reoperation for residual ventricular defects or inadequate relief of their pulmonary stenosis. All have been followed postoperatively and 10 recatheterized. Many have major extra cardiac lesions involving the brain, kidney, gastrointestinal tract, or skeleton.

Transposition of the Great Arteries. In many series, transposition has comprised up to 20% of necropsy cases in cyanotic congenital heart disease under 1 year of age. Twenty-one cases of trans-

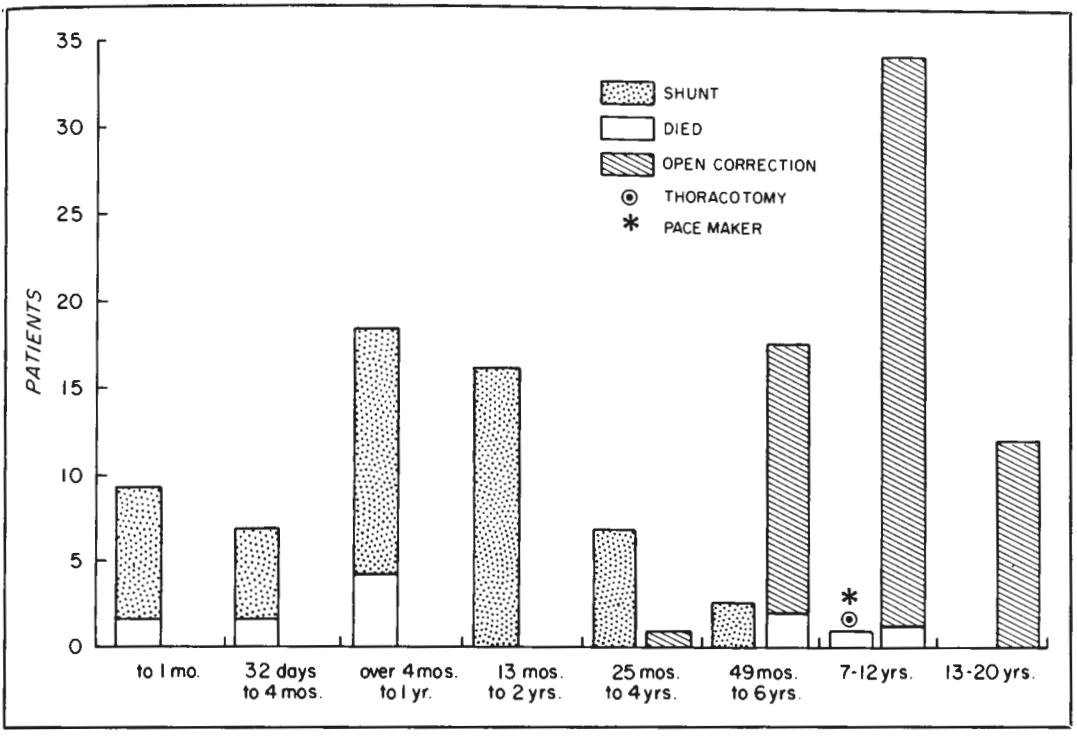

Fig. 1—Tetralogy of Fallot surgical therapy according to age.

position of the usual variety occurred in our series. Others associated with a single ventricle, bilocular heart, or tricuspid atresia are included with miscellaneous cyanotic lesions (Table IV).

All infants with transposition of the great arteries had palliative procedures in infancy, usually a balloon septostomy or a Blalock-Hanlon septectomy. In only two did the initial balloon septostomy produce adequate mixing. Usually the Blalock-Hanlon surgical procedure followed within a few weeks. Infants with associated ventricular septal defects required a concomitant pulmonary artery band and one with an associated ductus had it ligated. A palliative shunt was performed on two infants with associated pulmonic stenosis. The palliative procedures had a high risk. There were no deaths directly related to the balloon procedure. Four children have thus far had complete correction by the Mustard technique and improved postoperatively. One boy with residual pulmonary hypertension died this month, 33 months after the correction.

Miscellaneous Cyanotic Lesions. Fifty children with rarer cyanotic congenital defects were seen, of whom thirty-six were less than one year of age (Table V). Of the eleven cyanotic children with tricuspid atresia, nine were infants and two were older, with an age span from 1 day to 17 years.

TABLE IV
TRANSPOSITION OF THE GREAT VESSELS (21)

Procedures		Expired	Mortality %
Catheterization	11	0	0
Balloon			
Surgical			
Palliative	15		17.6%
Blalock–Hanlon 11		2	
Blalock–Hanlon and Banded Pulmonary Artery 2		1	
Shunts 2		0	
Correction		0	
Mustard 4			
Total Surgical Procedures	30		10%
Total Patients	21		14.2%

TABLE V
MISCELLANEOUS CYANOTIC LESIONS (50)

Defects		Patients	Expired
Tricuspid Atresia		11	1
Total Anomalous Pulmonary Venous Return		3	2
Single Ventricle		6	2
Banded	4		
Shunt with Pulmonic Stenosis	1		
Thoracotomy	1		
AV Canal		5	2
Splenic Syndromes		5	2
Multiple Mixed		20	14
Pulmonary Atresia	4		
Mitral Atresia	3		
Hypoplastic Right Heart	1		
Truncus	4		
Double Outlet Right Ventricle	2		
Ebstein's	3		
Hypoplastic Left Heart with Mitral Stenosis	2		
Multiple Defects	1		
Total		50	23

Nine required shunts to increase pulmonary blood flow, but two cases with unusually large pulmonary blood flow were palliated by banding the main pulmonary artery. The two older children had their second shunt created during the past year; one a 17-year-old high school senior has won a trip to Europe this summer on a singing tour.

The others are a discouraging group most of whom have been palliated by shunts or banding the pulmonary artery. A balloon septostomy did not significantly improve the condition of one child with pulmonary atresia. One atrio-ventricular canal was corrected and survived. A boy of 17 with a truncus arteriosus, Type I, had an attempted Rastelli procedure, but had irreversible pulmonary hypertension. The total mortality was 46%, but 36 were less than one year of age.

Conclusion. During the last six years, 557 children have had 593 surgical procedures for correction or palliation of their congenital heart defects with a mortality rate of 7.58%. One hundred fourteen patients were less than one year of age. Of the 368 acyanotic patients, 2.16% died at surgery or of related causes in the following month. Tetralogy of Fallot was the most favorable cyanotic lesion with a mortality for shunts in early childhood of 13% and for open correction of 63 patients it was 4.7%. Cooley's (Cooley and Hallman, 1966) recent review of his experience over a 10-year period reports the mortality for shunts as 7.2% and for open correction 15%. At Johns Hopkins University Hospital, 187 patients, ages 2 to 40 years, underwent complete correction of tetralogy in the last five years with a 9.6% mortality (Bender, *et al.*, 1970).

Our study showed 18 of 21 children with transposition of the great arteries survived. While other children with complex cyanotic lesions had a 46% mortality, this included many high-risk infants in whom an aggressive approach for palliation was justified because their prognosis was, otherwise, hopeless.

Advances in cardiac surgery have been great in the last 30 years, but further progress is anticipated, especially in infants. A cooperative effort involving referring physicians, pediatric cardiologists, physiologists, anesthesiologists, surgeons, and intensive care nurses is required to continue this trend.

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